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DIAGNOSIS OF PULMONARY STENOSIS BY ANGIOCARDIOGRAPHY

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THE development of improved methods for the diagnosis of congenital pulmonary stenosis has become increasingly important since surgical procedures for the relief of this condition have been introduced. In addition to physical examination and roentgenographic study of the cardiac silhouette and lung fields, cardiac catheterization, oxygen consumption studies, and oximetry have proved to be valuable diagnostic aids and have achieved general acceptance. Although these studies can be carried out with relative ease on large children and adults, many technical difficulties arise when they are applied to infants. Serial contrast visualization of the cardiac chambers and great vessels (angiocardiography) has been advocated by Castellanos,[1, 2] Sussman,[3, 4, 5] and others[6-15] and employed by them to elucidate abnormalities present in the cardiopulmonary circulation. Although these workers have found the technique to be of great diagnostic value, it has not been widely used in spite of its many advantages. The direct information as to the course of intracardiac blood flow and relative size and location of the cardiac chambers and great vessels which can be obtained with angiocardiography has been of aid to us in establishing the exact diagnosis in several types of congenital cardiac anomalies and has been particularly helpful in differentiating the various types in which cyanosis is a prominent symptom. The method has the further advantage of being applicable to patients of all ages; diagnostic radiograms are obtained as easily in small infants as in children and adults.

PROCEDURE

In order to visualize cardiac abnormalities satisfactorily by angiocardiography, it is necessary to have equipment capable of producing a rapid sequence of radiographic exposures. Such newer automatized radiographic techniques as the tautograph* developed by one of us (W. G. S.) make this possible. The tautograph makes ten radiographic exposures within a period of ten seconds.

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*A description with mechanical details is in the process of publication in the American Journal of Roentgenology and Radium Therapy.

Each patient is fasted for a period of at least four hours before the procedure. Infants and children too small to cooperate are given a general ether anesthetic. In older patients the entire operation is carried out under local Novocain anesthesia without general sedation. In patients with cyanotic heart disease and polycythemia, subcutaneous fluids are administered preoperatively to prevent dehydration, and oxygen is given concomitantly with the anesthetic.

The patient is placed on the tautograph, and with sterile technique the left or right antecubital vein is isolated by a routine cut-down procedure. The distal end is ligated, and a No. 13 or 14 cannula is inserted into the proximal end and tied in place. A slow intravenous drip of saline solution is begun through a three-way stopcock to insure patency of the cannula. The patient is placed in proper position on the table and a few minims of 70 per cent Diodrast injected through the cannula. If after several minutes no reaction has occurred, the final injection is made. Infants 3 months to 2 years of age receive 10 to 18 c.c. of Diodrast; children 2 to 10 years, 20 to 30 c.c.; and children 11 to 15 years, 30 to 40 c.c. The injection must be made as rapidly as possible in order to obtain a sufficiently dense concentration of Diodrast to insure good contrast. An injection period of longer than two seconds will seldom give sufficient contrast for diagnostic visualization of the heart or great vessels. The injection is begun immediately after the first exposure has been made.

Immediately following the injection, in the anesthetized patients, there is frequently seen a momentary irregularity of respiratory movements. In the unanesthetized patient there is often a transient feeling of increased heat, retching, and faintness. As soon as possible after the injection, the cannula is removed, the vein tied off, and the wound closed with silk sutures.

RESULTS

In order properly to interpret films showing abnormalities, it is necessary to be familiar with the normal configuration of the heart chambers and great vessels. The two most useful views are the left anterior oblique and the anteroposterior. A sequence of exposures showing the left anterior oblique view in a normal subject is shown in Figs. 1 through 6. Fig. 1 shows Diodrast immediately after injection, passing down the superior vena cava to the right auricle, into the right ventricle, and beginning to appear in the pulmonary conus where it is arching upward and backward. Fig. 2 shows better filling of the right ventricle, a fully distended pulmonary conus, and a normal-sized left and right pulmonary artery. No Diodrast is being injected in Fig. 3, and there is very good filling of the right ventricle, pulmonary conus, and pulmonary arteries. In Fig. 4 the opacification of the right side of the heart and pulmonary arteries has almost faded, but the pulmonary veins, left auricle, and left ventricle can be seen distinctly. In Fig. 5 the opacification of the right side of the heart and pulmonary arteries has disappeared. The pulmonary veins, left auricle, left ventricle, aorta, and great vessels are clearly visualized. Fig. 6 shows the same structures seen in the preceding film except that the aorta and its branches are more sharply defined, and the pulmonary veins are less distinct.

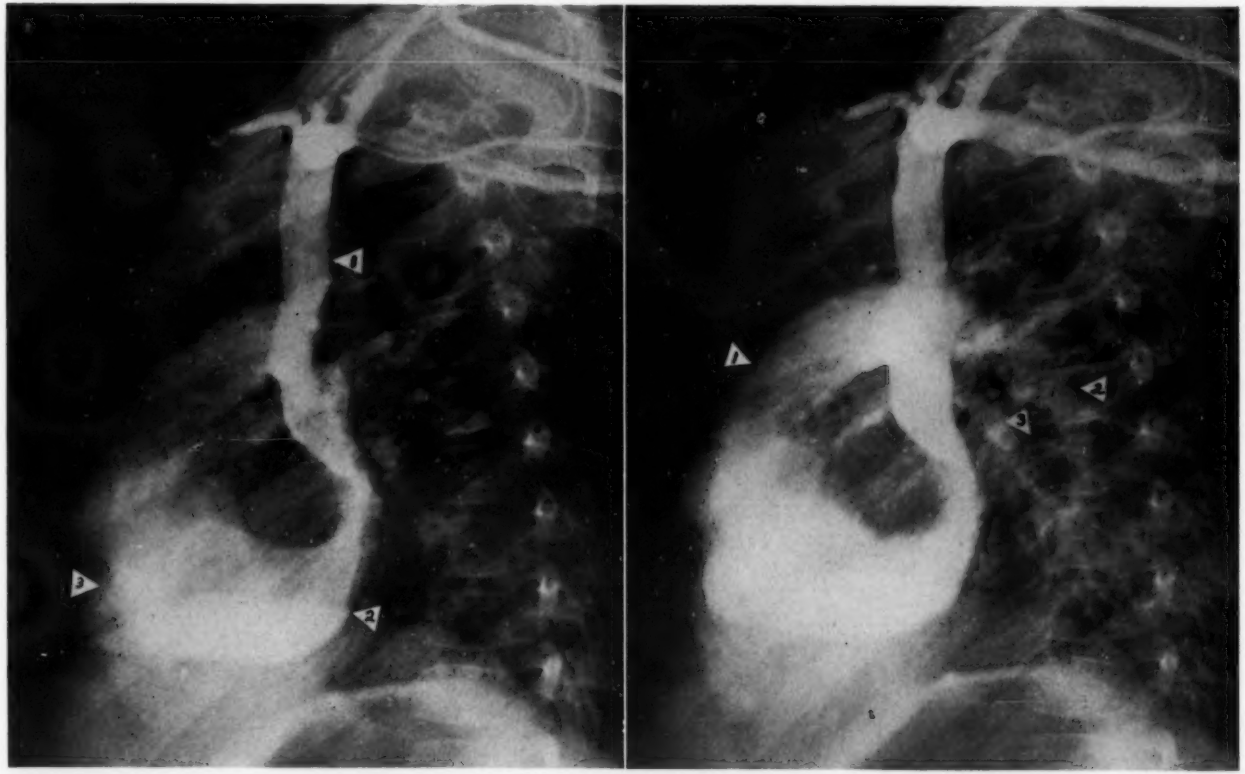

Fig. 1. Fig. 2.

Fig. 1.—Normal angiocardiogram, left anterior oblique. *1*, Superior vena cava. *2*, Right auricle. *3*, Right ventricle.
Fig. 2.—Normal angiocardiogram, left anterior oblique. *1*, Pulmonary conus. *2*, Left pulmonary artery. *3*, Right pulmonary artery.

Fig. 3.

Fig. 4.

Fig. 3.—Normal angiocardiogram, left anterior oblique.
Fig. 4.—Normal angiocardiogram, left anterior oblique. *1*, Pulmonary vein. *2*, Left auricle. *3*, Left ventricle.

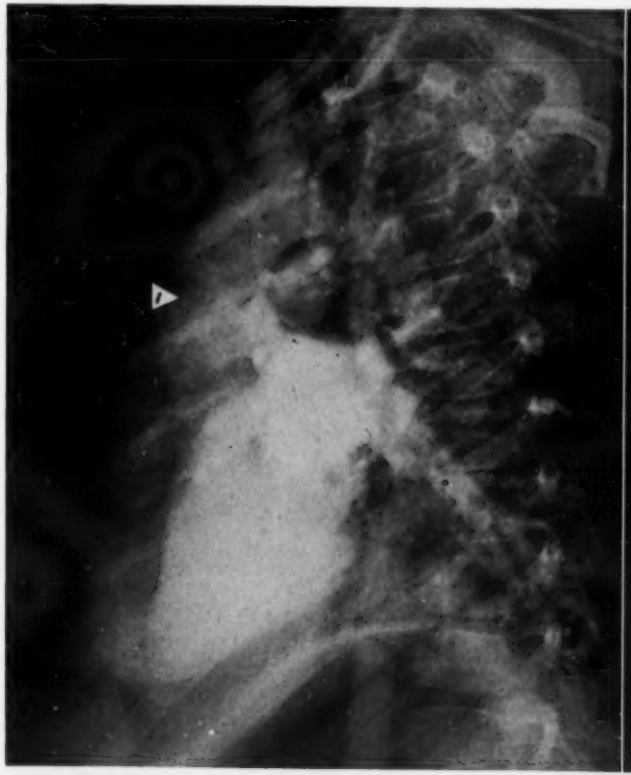

Fig. 5.

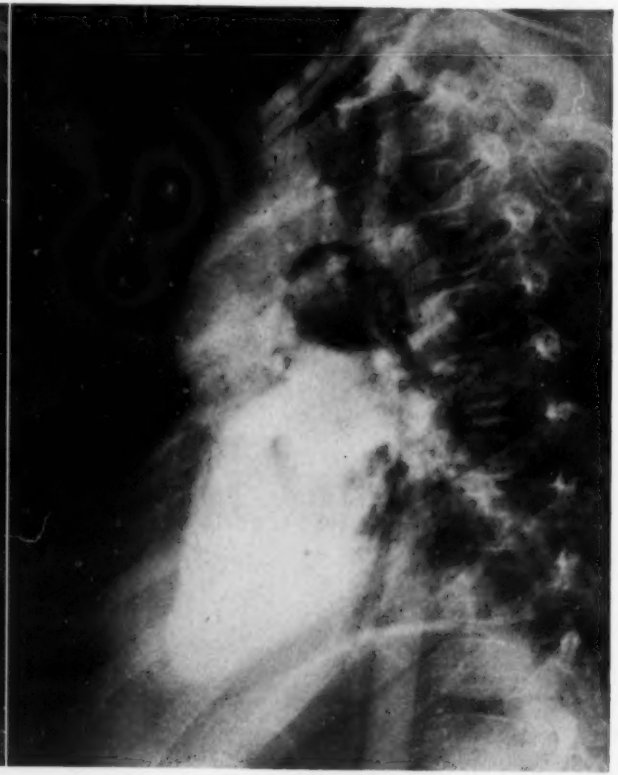

Fig. 6.

Fig. 5.—Normal angiocardiogram, left anterior oblique. *1*, Ascending aorta.
Fig. 6.—Normal angiocardiogram, left anterior oblique.

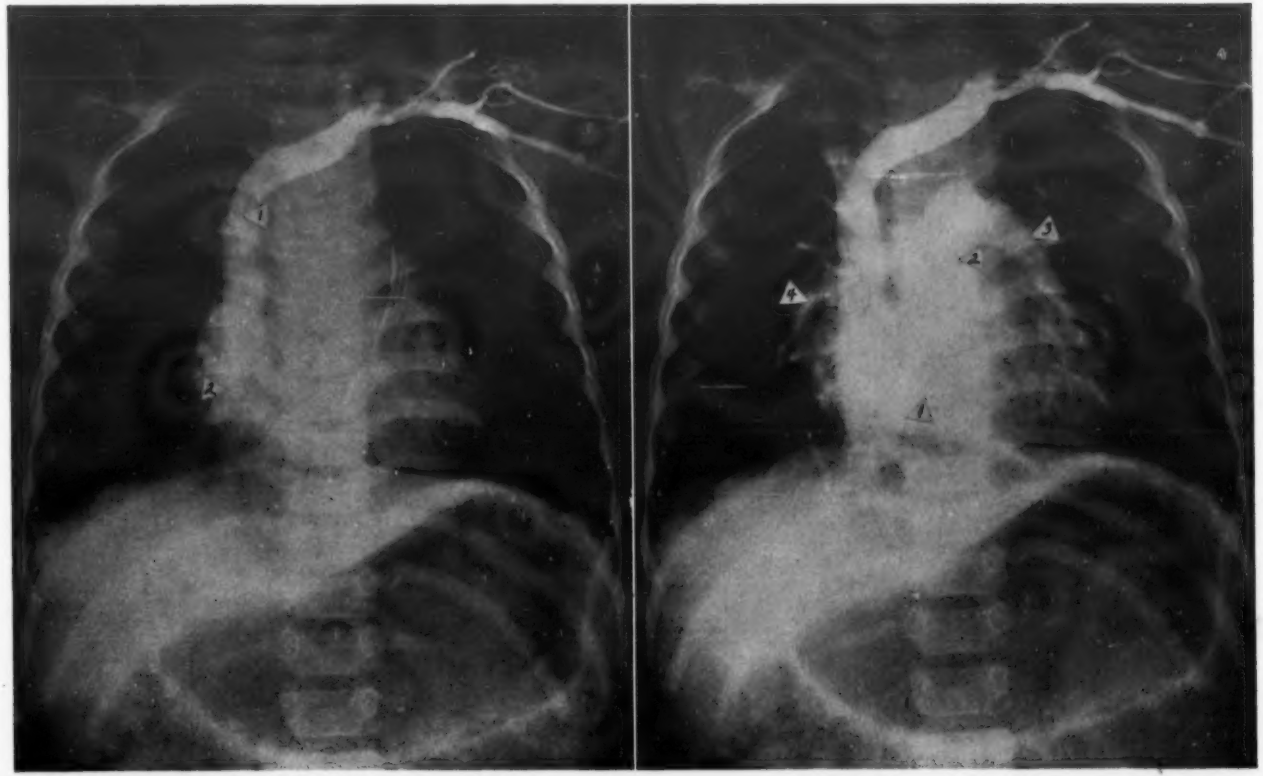

Fig. 7. Fig. 8.

Fig. 7.—Normal angiocardiogram, anteroposterior. *1*, Superior vena cava. *2*, Right auricle.

Fig. 8.—Normal angiocardiogram, anteroposterior. *1*, Right ventricle. *2*, Pulmonary artery. *3*, Left pulmonary artery. *4*, Right pulmonary artery.

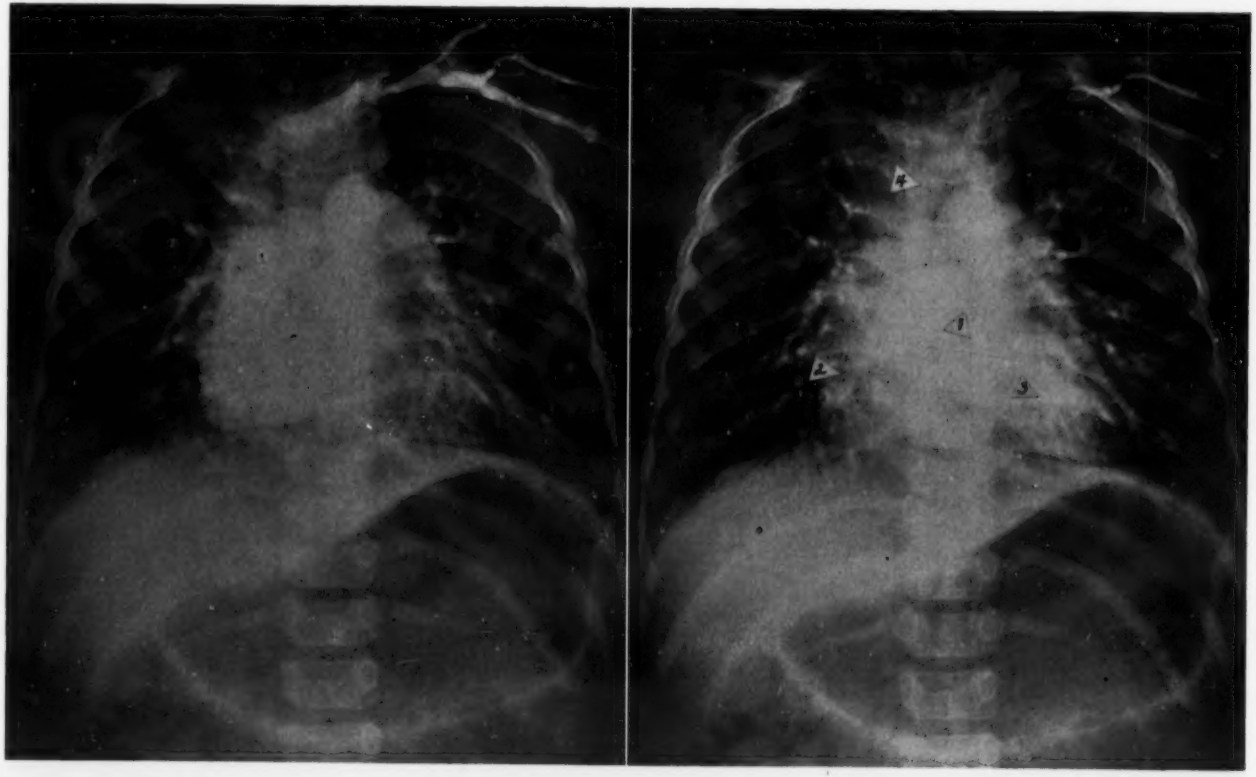

Fig. 9.

Fig. 10.

Fig. 9.—Normal angiocardiogram, anteroposterior.
Fig. 10.—Normal angiocardiogram, anteroposterior. *1*, Left auricle. *2*, Pulmonary vein. *3*, Left ventricle. *4*, Aorta.

Fig. 11.

Fig. 12.

Fig. 11.—Normal angiocardiogram, anteroposterior.
Fig. 12.—Normal angiocardiogram, anteroposterior. *1*, Left auricle.

The normal sequence in the anteroposterior view is shown in Figs. 7 through 12. Fig. 7 shows Diodrast entering through the left antecubital vein into the superior vena cava and just beginning to fill the right auricle. Fig. 8 shows complete filling of the right auricle and right ventricle. The pulmonary conus extends upward. The pulmonary artery and its bifurcation are seen at the apex of the conus, and both right and left pulmonary arteries are fully distended. As pointed out by others,[16] the left pulmonary artery is seen to constitute that portion of the left cardiac border between the aortic and ventricular shadows. Fig. 9 shows a decrease in the amount of Diodrast being injected but reveals the whole right side of the heart with the pulmonary arteries in sharp relief. In Fig. 10 only a small amount of Diodrast remains in the right auricle and ventricle, and the pulmonary arteries are less well visualized than in the preceding film. The pulmonary veins, however, may be seen emptying into the centrally located left auricle, with some Diodrast being seen in the left ventricle, which is contracted in systole. The aortic arch and great vessels can also be seen. Fig. 11 fails to reveal evidence of any Diodrast in the right side of the heart or pulmonary arteries. The pulmonary veins, left auricle, left ventricle, aorta and its branches are well outlined. In Fig. 12 the same structures are visualized as in the preceding film except that the left ventricle is in systole and is not seen. The central position of the left auricle, as described previously,[17] is well illustrated. It is thus shown conclusively that normally the left auricle constitutes no part of the left cardiac border.

Although it has been demonstrated that pulmonary arteries can be clearly visualized in both the anteroposterior and left anterior oblique views, the latter view is preferred since the shadows of the pulmonary arteries and aorta are separated in this position. This is essential in those types of cardiac abnormalities in which pulmonary arteries and aorta fill simultaneously.

Radiograms of four patients illustrate the value of angiocardiography in differentiating various types of cyanotic congenital heart disease.

NONFUNCTIONING RIGHT VENTRICLE WITH TRICUSPID STENOSIS

This patient, R. D., aged 14 months, was admitted with a congenital cardiac abnormality of the cyanotic type. Radiographic examination revealed a small right ventricle of the contour described by Taussig[18] as characteristic of cases of nonfunctioning right ventricle; the electrocardiogram showed left axis deviation. Angiocardiograms were done with the patient in both the anteroposterior and left anterior oblique position. The anteroposterior roentgenograms obtained are shown in Figs. 13 to 15. Fig. 13 was taken just after the injection was begun and shows the superior vena cava and right auricle in their normal position. No opaque material is seen in the expected region of the right ventricle. In the center, overlying the spinal column, is the circular left auricle and just to the left of and below this structure can be seen the opacification of the left ventricle. Fig. 14 shows the same structures; in addition, reflux filling of the hepatic veins is observed. Lying to the left of the superior vena cava are the ascending aorta and aortic arch, and in the concavity of the arch is the upper portion of the pulmonary artery. Fig. 15 shows more clearly the aorta with its major branches.

Fig. 13.

Fig. 14.

Fig. 13.—Nonfunctioning right ventricle with tricuspid stenosis, anteroposterior. *1*, Right auricle. *2*, Left auricle. *3*, Left ventricle.
Fig. 14.—Nonfunctioning right ventricle with tricuspid stenosis, anteroposterior. *1*, Hepatic veins. *2*, Ascending aorta. *3*, Pulmonary artery.

Fig. 15.

Fig. 16.

Fig. 15.—Nonfunctioning right ventricle with tricuspid stenosis, anteroposterior.
Fig. 16.—Nonfunctioning right ventricle with tricuspid stenosis, left anterior oblique. *1*, Left ventricle. *2*, Ascending aorta. *3*, Pulmonary artery. *4*, Hepatic veins.

The main pulmonary artery is easily seen with the right and left pulmonary arteries also visualized. Both the main pulmonary artery and its branches are smaller than normal.

Fig. 16 represents the first radiogram taken in the left anterior oblique position after the injection was partially completed. It shows complete opacification of the ventricular area. The aorta and its branches are filled, and the small pulmonary conus and pulmonary arteries can be seen. There is some reflux of opaque material into the hepatic veins.

The flow of Diodrast as demonstrated by these films is from the superior vena cava into the right auricle and then to the left auricle and into the enlarged left ventricle. Both the normal aorta and the small pulmonary conus appear to come off the left ventricle and fill simultaneously with Diodrast. The pulmonary arteries are smaller than normal. The failure of the right ventricle to visualize demonstrates either that this chamber is absent or is occluded from the circulation by an atresic tricuspid valve.

At operation pulmonary stenosis was found. Anastomosis of the left pulmonary artery to the aorta resulted in an improved pulmonary circulation with relief of the cyanosis and polycythemia.

PERSISTENT TRUNCUS ARTERIOSUS

This 16-month-old child, J. H., was admitted with congenital heart disease of the cyanotic type. Radiograms revealed marked enlargement of the heart, especially of the right ventricle. The shelflike projection of the right ventricle imparted to the organ that contour which has been described as characteristic of cases of persistent truncus arteriosus.[19] The electrocardiogram gave evidence of right axis deviation. Angiocardiograms were taken in both anteroposterior and left anterior oblique positions. Figs. 17 and 18 show the latter view. In Fig. 17 Diodrast can be seen entering the superior vena cava, right auricle, and right ventricle, whence it spills over into the left ventricle. The beginning of the common arterial pathway can be visualized. Fig. 18 shows a large opaque right ventricle with an increasing amount of opacification of the left ventricle. There appears to be a defect of the interventricular septum. A single arterial outflow (truncus arteriosus) is visualized. Neither pulmonary conus nor pulmonary artery is seen.

In the anteroposterior view, Fig. 19 shows opacification of the superior vena cava, right auricle, and partially of the right ventricle. Fig. 20 shows full filling of the right ventricle with partial filling of the left ventricle apparently through a large interventricular septal defect. The single arterial pathway is beginning to be visualized. Fig. 21 shows opacification of both ventricles and the whole truncus, which is seen to lie on the right. Very small pulmonary arteries are seen, apparently arising from the common truncus.

On the basis of these studies it is felt that this patient had a persistent truncus arteriosus with very small pulmonary arteries and a large interventricular septal defect.

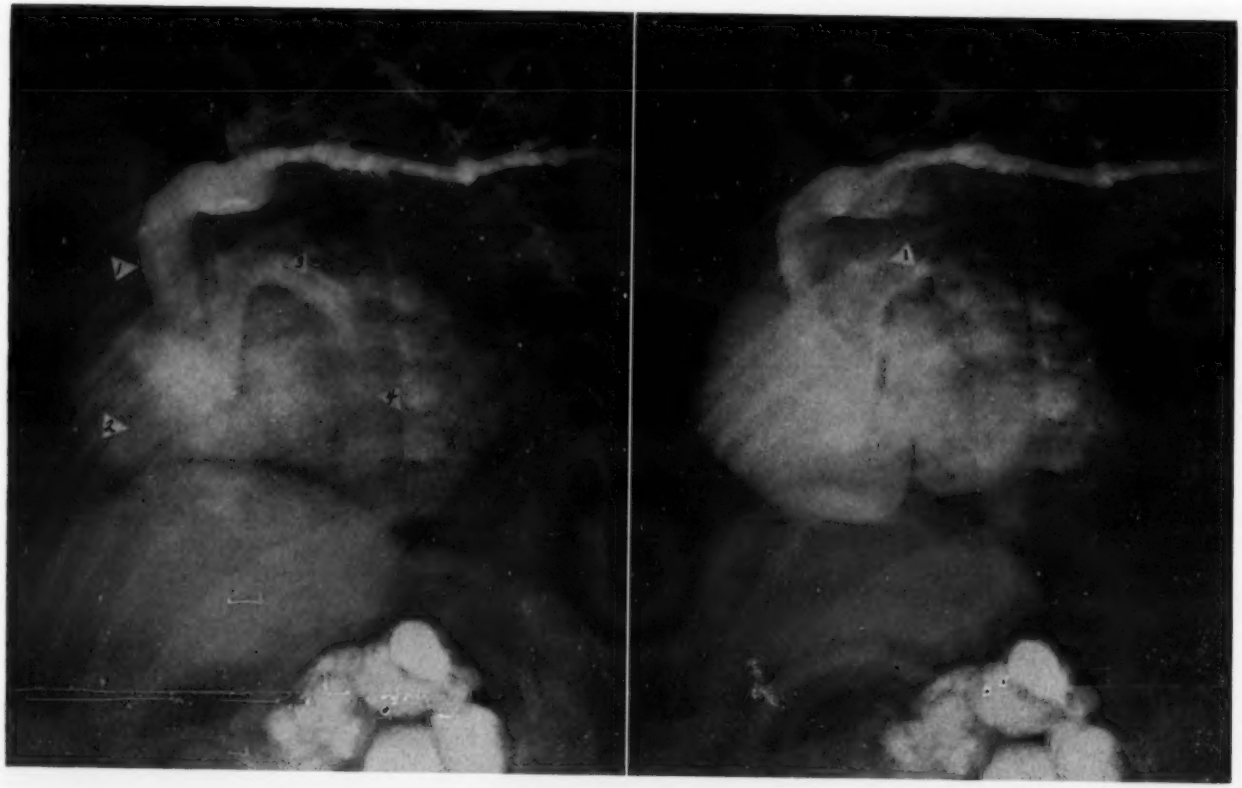

Fig. 17.

Fig. 18.

Fig. 17—Persistent truncus arteriosus, left anterior oblique. *1*, Superior vena cava. *2*, Right ventricle. *3*, Truncus arteriosus. *4*, Left ventricle.

Fig. 18.—Persistent truncus arteriosus, left anterior oblique. *1*, Truncus arteriosus.

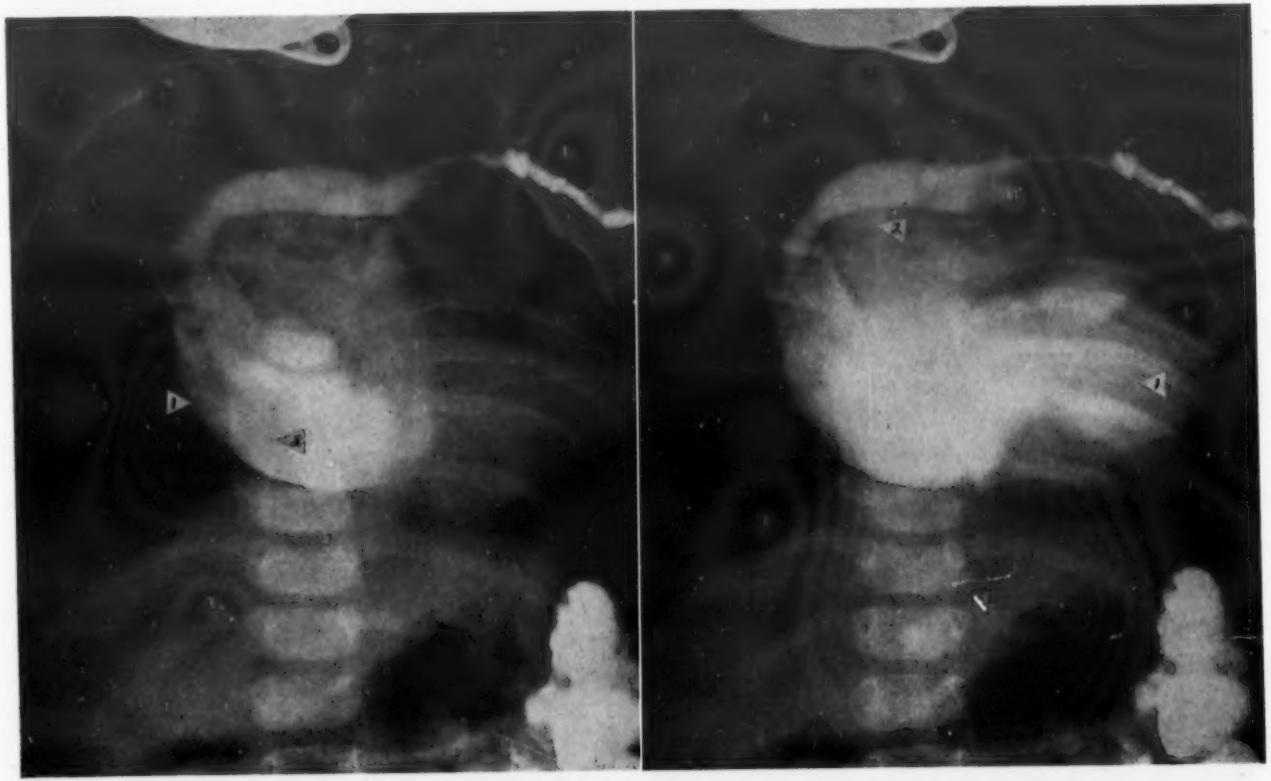

Fig. 19. Fig. 20.

Fig. 19.—Persistent truncus arteriosus, anteroposterior. *1*, Right auricle. *2*, Right ventricle.
Fig. 20.—Persistent truncus arteriosus, anteroposterior. *1*, Left ventricle. *2*, Truncus arteriosus.

Fig. 20.—Persistent truncus arteriosus, anteroposterior. *1*, Left ventricle. *2*, Truncus arteriosus.

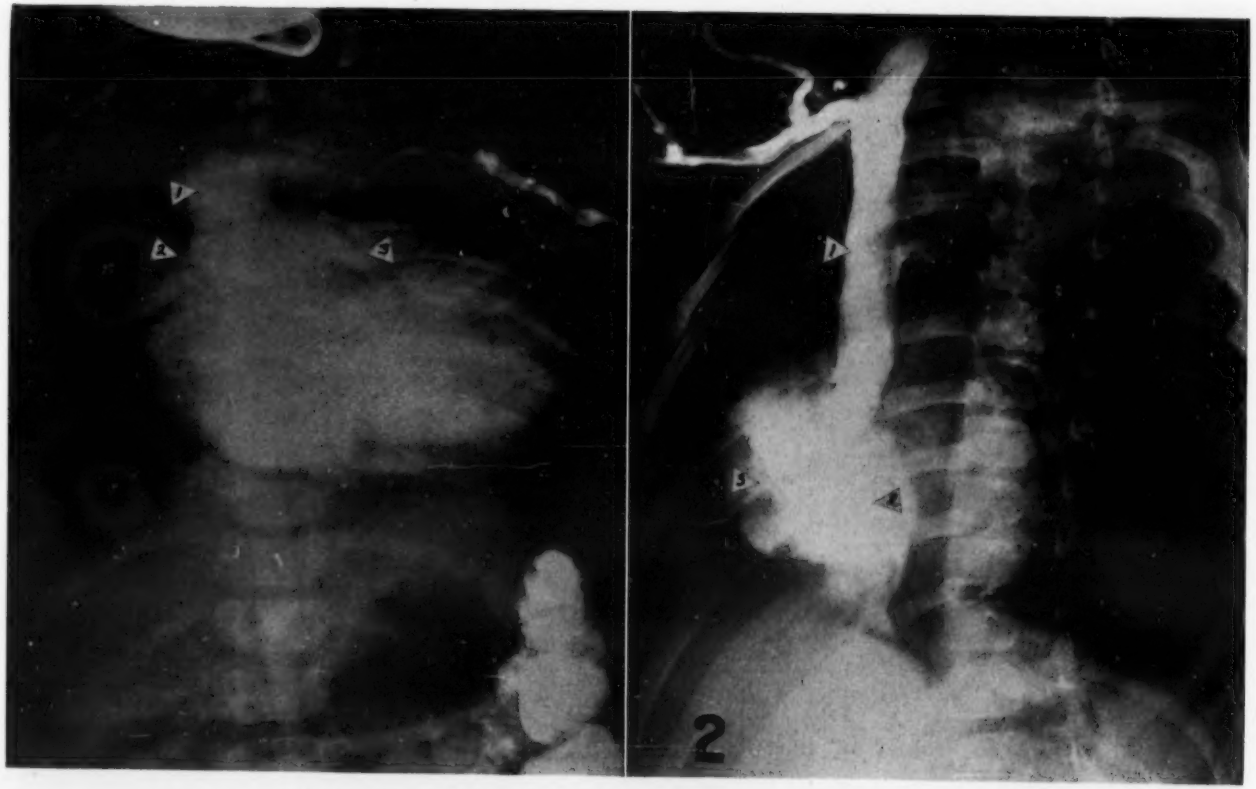

Fig. 21. Fig. 22.

Fig. 21.—Persistent truncus arteriosus, anteroposterior. *1*, Truncus arteriosus. *2*, Right pulmonary artery. *3*, Left pulmonary artery.
Fig. 22.—Tetralogy of Fallot, left anterior oblique. *1*, Superior vena cava. *2*, Right auricle. *3*, Right ventricle.

Fig. 23. Fig. 24.

Fig. 23.—Tetralogy of Fallot, left anterior oblique. *1*, Left ventricle. *2*, Main pulmonary artery. *3*, Aortic arch.
Fig. 24.—Tetralogy of Fallot, left anterior oblique. *1*, Left pulmonary artery. *2*, Aortic arch.

TETRALOGY OF FALLOT

This 12-month-old boy, P. D., was admitted with a tentative diagnosis of tetralogy of Fallot. Radiograms showed decreased pulmonary vascular markings, right ventricular enlargement, slight concavity in the region of the pulmonary conus, and a clear aortic window. Right axis deviation was seen in the electrocardiogram.

Angiocardiograms taken in the left anterior oblique position are seen in Figs. 22 to 24. In Fig. 22 there is opacification of the superior vena cava, right auricle, and right ventricle. Fig. 23 shows the same structures, and in addition beginning opacification of the left ventricle is noted. A small pulmonary conus is seen in the normal position with very small left pulmonary arteries. A small amount of Diodrast can be seen in the ascending aorta and aortic arch. Fig. 24 shows increasing opacification of the left ventricle. The small pulmonary conus and stenotic right and left pulmonary arteries are more clearly seen. The entire length of the aorta can be seen.

The early filling of the left ventricle must occur because of the presence of an interventricular septal defect. The abnormally small size of the pulmonary arteries is directly demonstrated. An overriding aorta is indicated by the simultaneous filling of the pulmonary arteries and aorta. Pulmonary stenosis was confirmed at operation.

DISCUSSION AND CONCLUSIONS

Angiocardiography has been safely utilized by numerous workers as a diagnostic aid in many cardiac conditions. It is felt this method is of great value in infants and children who are so small that cardiac catheterization is impossible or impractical. By this method one can accurately trace the course of the circulation through the heart chambers and visualize the relative size, location, and number of the great vessels.

All of the cardinal features of the tetralogy of Fallot are demonstrated in the angiocardiogram: (1) an interventricular septal defect is indicated by Diodrast flowing directly from the right ventricle into the left ventricle, producing increasing opacification of the latter in the second or third radiogram; (2) simultaneous opacification of the aorta, pulmonary conus, and pulmonary arteries indicates the presence of an overriding aorta with the Diodrast flowing simultaneously into both the aorta and pulmonary conus from the right ventricle; (3) the enlargement of the right ventricle is seen; (4) the decreased caliber of the pulmonary arteries is directly visualized. This last observation alone will serve to differentiate cases of tetralogy of Fallot from those of Eisenmenger's complex. In the latter condition pulmonary arteries of normal or unusually large size are seen (Fig. 25).

Cases of nonfunctioning right ventricle with tricuspid stenosis are characterized by the following findings: opaque material can be observed to enter the right auricle from the superior vena cava. None can be seen going into the right ventricle, but instead it can be seen entering the left auricle and then an enlarged left ventricle. Following this there is simultaneous visualization of the

Fig. 24.—Tetralogy of Fallot, left anterior oblique. 1, Left pulmonary artery. 2, Aortic arch.

aorta, and if pulmonary stenosis is present, small pulmonary arteries are visualized.

Persistent truncus arteriosus with stenotic pulmonary arteries will show the following characteristics: (1) the Diodrast reveals a very large right ventricle; (2) a large interventricular septal defect is indicated by rapid opacification of the left ventricle in the second or third radiogram; (3) in the second or third

Fig. 25.—Eisenmenger's complex, left anterior oblique. *1*, Ascending aorta. *2*, Main pulmonary artery. *3*, Left pulmonary artery.

radiogram a single large vessel is seen emerging from the region of the ventricles, and because very rapid opacification of this vessel occurs at the same time the left ventricle begins to be visualized, it is likely that the truncus overrides the septal defect; (4) no pulmonary conus is seen, but abnormally small pulmonary arteries can be visualized arising from the single large truncus. We have not studied a case of persistent truncus in which the pulmonary blood flow is derived from the bronchial arteries.

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ECZEMA VACCINATUM: RECOVERY OF VACCINE VIRUS FROM THE CUTANEOUS LESIONS OF TWO CHILDREN AND THE DEMONSTRATION OF AN ANTIBODY RISE DURING CONVALESCENCE

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KAPOSI'S varicelliform eruption[1] is a syndrome in which individuals develop an eruption and a febrile reaction as a complication of a pre-existing eczema. In many of these individuals the secondary eruption is the result of primary infection with the virus of herpes simplex,[2-5] but vaccine virus may also enter the eczematized skin and cause a clinically similar picture, eczema vaccinatum. Diagnosis of eczema vaccinatum has been confirmed by the demonstration of Guarnieri bodies in the lesions or in the tissues of inoculated rabbits[6-12] or was made because of a history of exposure to vaccinia.[8-22] Few attempts have been made to identify the virus by cross-immunity studies and none to show an antibody rise in the blood of the patient during convalescence. The present report describes the recovery of vaccine virus from the acute skin lesions of two patients and the subsequent development of neutralizing antibodies against vaccinia in both patients during convalescence.

CASE 1.—C. C., a 3½-year-old Negro child, had had a generalized atopic dermatitis most marked on the face, forearms, and legs since the age of 2 years. Three days before admission to the Cincinnati General Hospital on Nov. 6, 1947, a small papular lesion was noted on the face. New lesions rapidly appeared over the face and later on the neck, arms, and legs. The mother applied penicillin ointment but the lesions progressed, the face became edematous, and fever developed. On admission the child appeared acutely ill. There was evidence of a chronic, lichenified dermatitis on the arms and legs. Over the face, arms and thighs discrete vesiculopustular, umbilicated lesions were seen (Fig. 1). The temperature was 105° F., the white blood count 16,000 with 88 per cent polymorphonuclear leucocytes. Swabs of the skin lesions taken on admission and inoculated on the scarified corneas of rabbits produced keratoconjunctivitis. In the course of the next four days the child's temperature gradually returned to normal, the lesions crusted and dried, leaving only depigmented areas and evidence of the old atopic dermatitis. No history of recent exposure to herpes or to vaccinia could be obtained. The child had not been vaccinated.

Identity of the C. C. strain.—Swabs of the patient's skin lesions taken on the day of admission were rubbed on the scarified corneas of rabbit 1. Panophthalmitis developed on the second day. The cornea and nictitating membrane of one eye were removed and after a portion of the cornea had been reserved for histologic section the tissues were pooled, ground in a mortar with saline and alundum, and centrifuged at low speed for a few minutes. A portion of the supernatant fluid was cultured on a blood agar plate and the remainder stored in the refrigerator. After twenty-four hours of incubation had revealed no

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bacterial growth, the material was rubbed with a swab on the scarified corneas of normal rabbit 2 and rabbit 3, which was immune to herpes. Panophthalmitis developed in both animals, indicating that an agent other than herpes simplex virus was present. The cornea and nictitating membrane of rabbit 2 were transferred by swab to the corneas of normal rabbit 4, and rabbit 5, which was immune to herpes, and injected intracerebrally into six mice. Again a reaction

Fig. 1.—C. C. Eczema vaccinatum.

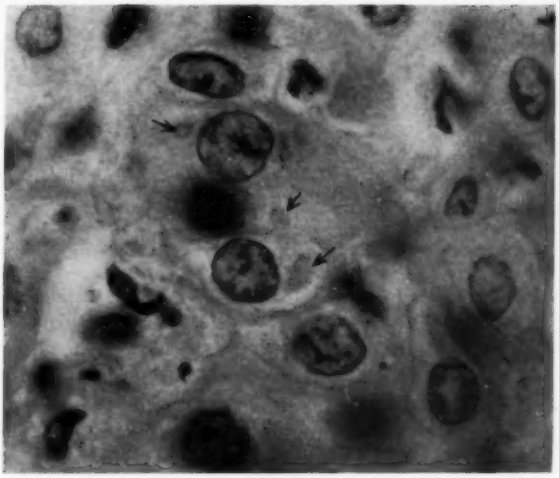

Fig. 2.—C. C. Eczema vaccinatum. Intracytoplasmic inclusions in rabbit's cornea. (Hematoxylin and eosin, ×1000)

occurred in the eyes of both rabbits. Sections of the corneas of rabbits 1 and 2 revealed numerous intracytoplasmic inclusions (Guarnieri bodies) characteristic of the vaccinia-variola group of viruses (Fig. 2). Intranuclear inclusions characteristic of herpes simplex were not observed. Subsequently rabbits 1, 2, and 4 were tested for immunity to the R.I. strain of vaccinia* by the combined ocular and cutaneous routes and were found to be immune. At a later date

two of these animals were challenged with the H.F. strain of herpes simplex* and were not immune. Thus it was apparent that the infectious agent recovered from the cutaneous lesions induced immunity in rabbits to vaccinia but not to herpes simplex virus. The mice injected intracerebrally remained well and a month later failed to resist cerebral challenge with herpes virus.

The results of cross-immunity tests in rabbits are summarized in Table I. Five normal control animals (1, 2, 4, 7, and 8) developed a reaction after inoculation with the C. C. strain of virus. After recovery they were immune to the R.I. strain of vaccinia. Two of these rabbits (1 and 2) were later tested for immunity to herpes virus but were not immune. Three animals (3, 5, and 6) that had previously withstood a challenge inoculation with a strain of herpes virus did not resist the C.C. strain. Rabbit 9, which had recovered from infection with the R.I. strain of vaccinia, was thereafter immune to the C.C. strain.

TABLE I. CROSS-IMMUNITY TESTS IN RABBITS

STRAIN INOCULATED	RABBIT NUMBER	PREVIOUSLY HAD RECEIVED	RESULT OF OCULAR INOCULATION			RESULTS OF IMMUNITY TESTS	
			PASSAGE INOCULATED	REACTION IN EYE	CYTOPLASMIC INCLUSIONS	VACCINIA (R.I. STRAIN) I. CUTANEOUS	HERPES SIMPLEX (H.F. STRAIN) I. OCULAR
C.C. Case 1	1	Nothing	Original	+	+	Immune	Not immune
	2	Nothing	I	+	+	Immune	Not immune
	3	H.F. herpes	I	+	--	----	----
	4	Nothing	II	+	--	Immune	----
	5	H.F. herpes	II	+	--	----	----
	6	H.F. herpes	III	+	--	----	----
	7	Nothing	III	+	--	Immune	----
	8	Nothing	III	+	--	Immune	----
	9	R.I. vaccinia	III	0	--	----	----
R.C. Case 2	10	Nothing	Original	+	+	Immune	Not immune
	11	Nothing	I	+	+	Immune	Not immune
	12	R.I. vaccinia	I	0	--	----	----
	13	R.I. vaccinia	I	0	--	----	----

An attempt to recover an infectious agent from the patient's blood was also made. Blood obtained on the day of admission was injected by the combined intracerebral (0.03 c.c.) and intraperitoneal (0.1 c.c.) method into four young mice. A month later they were tested for immunity to the H.F. strain of herpes, and were not immune. Serum which had been kept frozen in dry-ice was thawed after nine days and rubbed on the scarified corneas of a rabbit but there was no reaction.

Neutralization Tests.—Final proof of the infection of patient C.C. by the virus of vaccinia was obtained when it was shown that serum neutralizing antibodies developed during convalescence. Sera obtained on the day of admission and again fifteen days later were tested for their neutralizing ability against the R.I. strain of vaccinia. A 10 per cent lyophilized suspension of infected rabbit testis (centrifuged suspension in undiluted rabbit serum prepared in 1944) was rehydrated and dilutions of 1:50, 1:500 . . . etc., up to

*The R.I. strain of vaccinia and the H.F. strain of herpes simplex were kindly supplied by Doctor P. K. Olitsky of the Rockefeller Institute for Medical Research, New York.

1:50,000,000 made in 10 per cent rabbit serum-saline. The virus suspensions, when added to equal amounts (0.1 c.c.) of undiluted test sera, gave final dilutions of 1:100 (10^{-2}), 1:1,000 (10^{-3}) . . . etc., up to 1:100,000,000 (10^{-8}). The mixtures of virus dilution and serum were allowed to stand at room temperature for one-half hour. A rabbit with clear skin was clipped and its skin marked off with an indelible pencil. One-tenth cubic centimeter of each serum-virus mixture was injected intracutaneously into the marked areas and the resulting skin lesions were measured daily. Sterile skimmed milk was used as a control.

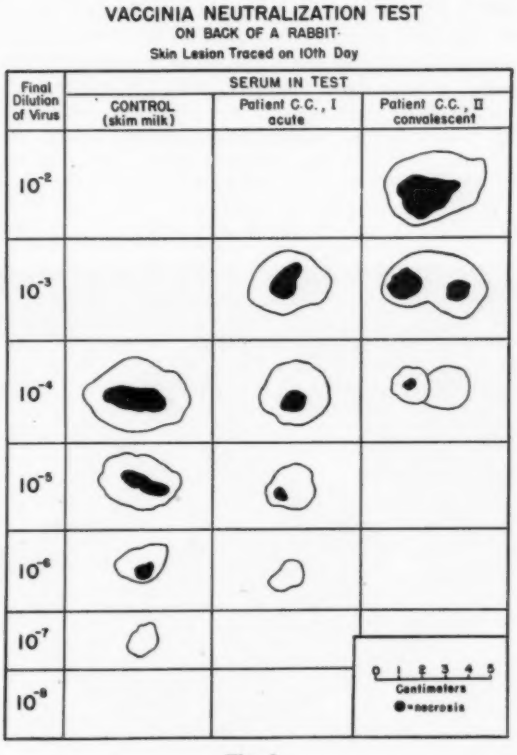

Fig. 3.

Lesions developed within a few days but no new ones appeared after the fifth day. Whereas the acute phase serum inhibited only the 10^{-7} dilution of virus, the convalescent phase serum modified the 10^{-4} dilution and completely suppressed the formation of all lesions in a dilution of 10^{-5} or above. A tracing made on the tenth day is shown in Fig. 3.

The same sera were examined for the presence of neutralizing antibodies against herpes simplex virus. Undiluted serum was mixed with equal amounts (0.2 c.c.) of decimal dilutions of herpes virus and after an incubation period of two hours at 37° C. the mixtures were injected intracerebrally into groups

of mice. The results showed that antibodies were absent in the acute phase serum and did not appear during convalescence.

CASE 2.—R. C., a 2-year-old boy, was admitted to the Cincinnati General Hospital on March 19, 1948, because of a large purulent lesion over the right eye with swelling of the eyelids of two days' duration. He had had eczema in the past and frequent attack of scabies. On admission the patient was moderately ill and very irritable. His temperature was 103° F., the white blood count 14,800. There was edema and cellulitis of both eyelids. Over the right eye including the eyebrow and bridge of the nose was a large lesion made up of discrete and confluent umbilicated pustules with several small satellite pustules (Fig. 4). There were other small pustules on the chin, face, neck, scalp, and index finger. Over the rest of the body were many scratches, the typical lesions of scabies, some indurated areas, probably the result of chronic eczema, and much secondary infection. The child was treated with moist compresses, penicillin, benzyl benzoate, and sulfathiazole ointment. The scabies rapidly improved but the lesion above the right eye progressed, the fever continued, and the child became worse. After 5 days the temperature fell to normal, the lesion gradually crusted over and healed. A swab of the cutaneous lesions taken five days after admission was rubbed on the scarified corneas of a rabbit and keratoconjunctivitis developed. The patient had been exposed to a recently vaccinated individual.

Fig. 4.—R. C. Eczema vaccinatum.

Identity of the R.C. Strain.—A swab of the lesion on the face taken five days after admission was rubbed on the scarified corneas of rabbit 10 and keratoconjunctivitis developed in three days. The cornea of one eye was removed and elementary bodies were observed in a scraping stained by Castañeda's method and in a histologic section of a portion of the cornea. The remainder of the cornea was ground in 2 c.c. of physiological saline and centrifuged lightly

for a few minutes. Culture of the supernatant fluid on blood agar revealed no bacterial growth. The material was inoculated by the combined intracutaneous and intraocular routes in rabbits. Rabbit 11, a normal control animal, developed a skin lesion, keratoconjunctivitis, and a febrile reaction while two rabbits immune to vaccinia, 12 and 13, were resistant. After recovery from infection with the R.C. strain rabbits 10 and 11 were immune to the R.I. strain of vaccinia but not to the H.F. strain of herpes (Table I).

The corneal suspension was also injected intracerebrally into six mice. The animals remained well. At the end of twelve days one mouse was sacrificed and its brain subinoculated intracerebrally into five other mice. These animals likewise remained well. At a later date both groups of mice were found to be not immune to cerebral challenge with herpes virus.

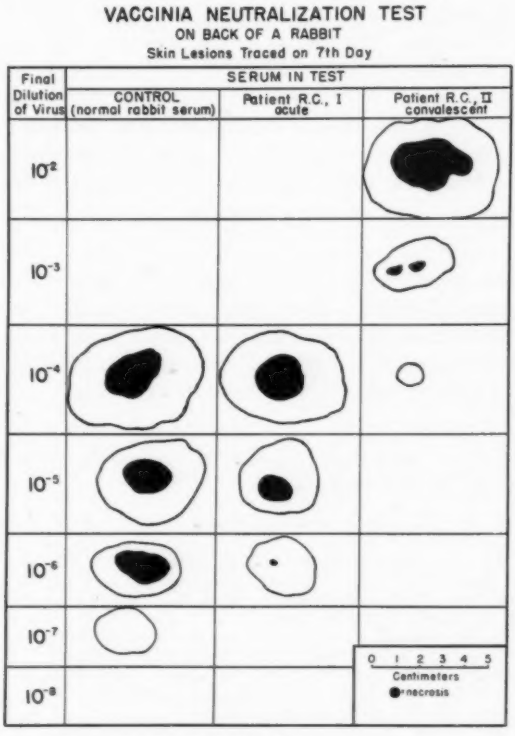

Fig. 5.

Neutralization Tests.—Acute phase serum obtained from the patient early in the course of the disease and convalescent phase serum obtained five weeks later were tested for the presence of neutralizing antibodies against vaccinia. The neutralization test was performed on the back of a rabbit, a lyophilized suspension of the R.I. strain of vaccinia being employed as before. Normal rabbit

serum was used as a control. The test (Fig. 5) showed that antibodies which were negligible in the acute phase serum developed during convalescence. Reactions to dilutions of 10^{-3} and 10^{-4} were modified and to higher dilutions completely inhibited. Antibodies against herpes virus were not found in the serum samples by the intracerebral neutralization test in mice.

DISCUSSION

Eczema vaccinatum occasionally occurs as a result of direct inoculation of an eczematous individual with vaccine virus,[22, 23] but more commonly arises as a result of exposure to a recently vaccinated child.[8-22] In a few instances vaccine virus has been recovered[11] or Guarnieri bodies demonstrated[6-12] in the skin lesions of the patient or in the tissues of inoculated rabbits. Apparently no attempts have been made to demonstrate a rise in neutralizing antibody titer during convalescence, although the presence of antibodies in a child after recovery has been recorded.[8] In the present report the diagnosis of eczema vaccinatum was made in two children by the recovery from the skin lesions of an agent which was shown to be a strain of vaccine virus by histologic and immunologic means. The relationship of this agent to the infection in the children was shown by the appearance in the blood stream during convalescence of neutralizing antibodies, which were not present at the onset of the acute eruption.

SUMMARY

An infectious agent was recovered from the cutaneous lesions of two children with eczema vaccinatum. Both agents were identified as a strain of vaccinia by the demonstration of cytoplasmic inclusions in the corneas of inoculated rabbits and the development of cross-immunity in rabbits. Each patient showed a rise in neutralizing antibodies against a known strain of vaccinia during convalescence.

Grateful acknowledgment is hereby made to Mr. Joseph Homan of the Department of Medical Art for preparing the photographs.

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STREPTOMYCIN IN THE TREATMENT OF PERTUSSIS

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THIS study was undertaken to determine the effect of streptomycin* on uncomplicated pertussis.

In 1945, Bradford and Day[1] found that streptomycin is an effective agent in the treatment of experimental infection produced in mice by fresh strains of *Hemophilus pertussis.*

Hegarty and associates[2] tested the activity of streptomycin in vitro against strains of *H. pertussis* and found that it was both bacteriostatic and bactericidal to this organism.

A review of the literature[3] at the time this study was started failed to reveal information on the effect of this agent against pertussis in humans. It was for this reason that the pilot study was undertaken. No attempt was made to compare this form of therapy with the use of human or rabbit hyperimmune serum.

PLAN OF STUDY

Only patients having uncomplicated whooping cough in either the catarrhal or early paroxysmal stage of the disease were included in this study. The patients were assigned in rotation to one of three groups. Those in the first group received streptomycin by the aerosol route; those in the second group received it intramuscularly, and those in the third received the usual symptomatic whooping cough treatment of the Cook County Contagious Disease Hospital. The latter were considered controls.

Before being assigned to a group, each patient was observed in the hospital for three days. Cough plates and blood counts were made, and the character, duration, and number of paroxysms were determined. A diagnosis of whooping cough was made only if the patient exhibited at least two of three diagnostic criteria: (1) positive cough plate; (2) a leucocytosis with a lymphocytosis; (3) typical paroxysms of coughing.

The patients were all observed in one ward. Nurses were assigned to this ward continuously. The nurses were specifically charged with the responsibility of timing each paroxysm as well as recording the number for each patient. They also noted whether or not emesis occurred and all other uncommon phenomena such as convulsions, epistaxis, cyanosis, and apnea. During the greater part of this study the nurses so assigned had no other duties. The usual nursing care was handled by other nurses in the ward. Upon completion of the three-day period of observation and upon having established a diagnosis of pertussis according to the above standards, therapy was started.

From the Contagious Division of the Cook County Hospital and the Department of Pediatrics, University of Illinois College of Medicine.

*Streptomycin Calcium Chloride Complex, very kindly supplied by Merck and Company, Inc.

Group 1 patients received one gram of streptomycin dissolved in 8 c.c. of normal saline solution. One cubic centimeter of this solution was administered every three hours around the clock. The solution was nebulized by attaching a Vaponefrin Nebulizer* to an oxygen tank, and administered via an infant-sized B.L.B. mask. The rate of flow of oxygen was 4 to 6 L. per minute and the average period of time to administer an aerosol dose of streptomycin was from seven to ten minutes.

Group 2 patients also received one gram (one million units) of streptomycin daily, divided into eight equal doses given intramuscularly every three hours.

Black and Poncher[5] have recently described an efficient and inexpensive mask which is being manufactured by the Vaponefrin Company. This would simplify the administration of aerosol therapy to the young infant.

RESULTS

Tables I to IV show that with the exception of one patient in the control group who died, practically all patients improved during their hospital stay. In those patients who received streptomycin, however, a more marked diminution in the average daily number of paroxysms occurred than in the control group. The average duration of paroxysms was also significantly different in the three groups.

The number and severity of complications exhibited in the control group were significantly greater than in the other groups. Two patients developed

TABLE I. AEROSOL TREATMENT

NAME	AGE	AVERAGE NO. PAROXYSMS DAILY BEFORE TREATMENT (3 DAYS)	AVERAGE NO. PAROXYSMS DAILY AFTER TREATMENT (7 DAYS)	AVERAGE DURATION BEFORE TREATMENT (SECONDS)	AVERAGE DURATION AFTER TREATMENT (SECONDS)	REMARKS
M. C.	9 mo.	25.0	8.0	20.0	27.3	
B. B.	4 yr.	12.6	1.8	20.1	7.2	Treatment stimulated paroxysms
R. E.	5 yr.	13.0	2.8	27.2	13.9	
T. J.	4 yr.	8.6	2.2	28.0	20.7	
B. S.	3 yr.	10.7	0.5	49.8	5.0	
J. P.	15 mo.	8.5	5.0	17.1	14.8	Twin
G. W.	10 mo.	23.9	9.0	56.6	50.0	
S. L.	3 yr.	10.0	4.8	26.4	28.2	

TABLE II. INTRAMUSCULAR TREATMENT

NAME	AGE	AVERAGE NO. PAROXYSMS DAILY BEFORE TREATMENT (3 DAYS)	AVERAGE NO. PAROXYSMS DAILY AFTER TREATMENT (7 DAYS)	AVERAGE DURATION BEFORE TREATMENT (SECONDS)	AVERAGE DURATION AFTER TREATMENT (SECONDS)	REMARKS
S. K.	6 mo.	18.7	7.6	35.5	40.0	Rash fourth day of treatment
L. D.	3 mo.	20.2	11.0	69.8	28.6	
L. S.	3 mo.	20.0	1.6	21.9	8.7	
J. L.	2 mo.	10.6	3.8	75.0	34.2	
S. G.	8 mo.	5.3	1.8	24.5	18.7	
N. M.	3 mo.	7.0	3.6	23.7	17.6	
F. K.	6 wk.	25.0	15.5	51.5	37.1	
R. W.	7 mo.	19.6	3.1	33.9	15.7	

*Nebulizers were very kindly supplied by the Vaponefrin Company of Chicago.

TABLE III. CONTROL

NAME	AGE	AVERAGE NO. PAROXYSMS DAILY BEFORE TREATMENT (3 DAYS)	AVERAGE NO. PAROXYSMS DAILY AFTER TREATMENT (7 DAYS)	AVERAGE DURATION BEFORE TREATMENT (SECONDS)	AVERAGE DURATION AFTER TREATMENT (SECONDS)	REMARKS
C. S.	5 yr.	6.0	8.4	12.8	21.3	Scarlet fever twelfth day
L. W.	3 yr.	19.0	9.3	53.6	36.5	Severe emesis
E. W.	6 yr.	13.6	9.5	70.7	46.2	Still vomiting on discharge
B. S.	4 yr.	24.5	11.2	54.3	67.3	Otitis media on tenth day
R. P.	15 mo.	10.0	10.0	18.9	37.3	Twin better
R. K.	2½ mo.	9.0	-	22.1	-	Died. Fifth day bronchopneumonia
A. W.	2½ yr.	12.0	3.1	27.8	34.1	Otitis media twelfth day
S. B.	18 mo.	9.0	8.7	21.6	26.2	

TABLE IV

	AVERAGE NUMBER OF PAROXYSMS PER DAY		AVERAGE DURATION OF PAROXYSMS PER DAY		NUMBER OF CHILDREN IN STUDY
	BEFORE TREATMENT (3 DAYS)	AFTER TREATMENT (7 DAYS)	BEFORE TREATMENT (3 DAYS)	AFTER TREATMENT (7 DAYS)	
Treatment:					
Aerosol	14.0	4.3	30.6	20.9	8
Intramuscular	15.8	6.0	42.0	25.1	8
Control	13.4	8.6	37.1	38.4	7 (One died)
Differences:					
Aerosol		- 9.7		- 9.7	
Intramuscular		- 9.8		-16.9	
Control		- 4.8		+ 1.3	
Per cent change:					
Aerosol		-69.3		-31.7	
Intramuscular		-62.0		-40.2	
Control		-35.8		+ 3.5	

otitis media which was treated with sulfadiazine and one infant developed bronchopneumonia and died in spite of oxygen, sulfonamide, and penicillin treatment.

One set of twins was observed. It was noted that the streptomycin-treated twin's disease ran a more benign course than the untreated twin, as he fed better, was not as apathetic, and had fewer and less severe paroxysms.

COMMENTS

While this is a small series of cases, it was thought by the investigators and nurses who observed each patient daily that the patients who received streptomycin via aerosol did much better clinically than the other two groups, despite the fact that the children had to be awakened to receive the treatment. This awakening frequently initiated a paroxysm. For this reason, the figures on the number and severity of paroxysms during the period of treatment are not recorded in this report, because they are misleading.

No toxic effects of the drug were noted with the exception of a transitory generalized morbilliform eruption which lasted two days in one patient who received streptomycin intramuscularly.

Since there had been no previous experience with streptomycin in whooping cough, our dosage of one gram a day and the length of treatment of one week was arbitrarily decided upon. From this pilot study, we believe there is sufficient evidence that streptomycin is of clinical benefit in the treatment of pertussis to justify more extended use. It also appears that the aerosol route of administration is the one of choice. This is in agreement with a statement recently made by Bradford.[4] One week of treatment appears to be sufficient in the average case. No attempt to evaluate untoward reactions on the vestibular function to streptomycin was made, because treatment was only administered for one week.

The decrease in the number of paroxysms, the lessening of the severity of the paroxysms, the marked decrease in complications, and especially the clinical impression obtained by trained observers, all attest to the efficacy of therapy with streptomycin, especially when given by the aerosol route.

CONCLUSIONS

1. Streptomycin appears to be an effective therapeutic agent in the treatment of pertussis.
2. The aerosol route of administration is the method of choice.
3. No untoward results were noted after one week of therapy.

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VENOUS PRESSURES IN CHILDREN IN HEALTH AND DISEASE

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SINCE the original determination of venous pressure by Stephen Hales[1] in 1767, little data pertinent to this measurement in children have accumulated.[2-4] In 1916 Hooker,[2] in studying the influence of age upon venous pressure, made observations in children, using an indirect method in which the end point was determined by noting the collapse of a vein. Lambert[3] found the mean venous pressure in children, using the direct method of Moritz and Tabora[5] to be 48.4 mm. of water. Jacques[4] using the same method determined the venous pressure on thirty-six children whose ages ranged from 7 to 15 years. His mean value was 48.3 mm. of water with a standard deviation of 15.2. Prior to 1943, most direct methods were impractical for determining venous pressure in children because of the large needles necessary for its determination.[6] The phlebomanometer described by Burch and Winsor[7] proved suitable mainly because of the small needle which could be employed. The instrument is small, simple to use, and may be placed on an adjoining table near the patient. Blood loss is negligible. Multiple determinations may be made employing small veins. It is a practical portable instrument suitable for office use.

The indications for accurate direct venous pressure measurements are numerous. They are essential for: (1) the proper evaluation and treatment of many clinical syndromes such as right ventricular failure, venous obstruction, shock, edema, and disturbed water balance; (2) accurate diagnosis; (3) early and objective evaluation of therapy; (4) following the course of certain clinical states; and (5) determining prognosis. Being objective, venous pressure measurements are free from the inaccuracies of many subjective procedures.

It is the purpose of this report to: (1) establish normal values for venous pressures in children using an accurate, practical, direct venous pressure method; and (2) compare venous pressures in normal children with venous pressures in patients with rheumatic heart disease without evidence of congestive heart failure and in patients with other disease states.

METHODS AND MATERIALS

Fifty children between the ages of 3 and 10 years, with normal cardiovascular systems, were studied. In addition the following children were studied: Thirteen children with rheumatic heart disease without evidence of congestive heart failure, and four children with glomerulonephritis, one of whom showed evidence of myocardial damage but no clinical evidence of congestive failure. The subjects rested at least thirty minutes prior to venous pressure measurement, then were placed on a firm table in the supine position. The phlebostatic

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level[8, 9] was determined, using a centimeter ruler and level. The level was placed at the fourth intercostal space and the anteroposterior diameter was measured, taking the distance from the lower portion of the level to the bed. The arm was placed at an angle of 45 degrees from the body so that the antecubital vein in which the venous pressure was to be measured was horizontal with one-half the anteroposterior chest diameter. This has been referred to as the phlebostatic level.[8, 9] No talking or breath-holding was permitted. The measurement was taken using a small-gauge needle which was inserted in the direction of the blood flow.

The instrument employed recorded venous pressure in millimeters of water. A pressure-balancing bulb allowed accurate determination of the venous pressure. The size of the needle was not of great importance to the accuracy of the readings, as all readings were made when no flow of fluid in the instrument was present. A No. 25 or 26 needle was ordinarily utilized. From three to six consecutive readings were taken and the lowest pressure was recorded.

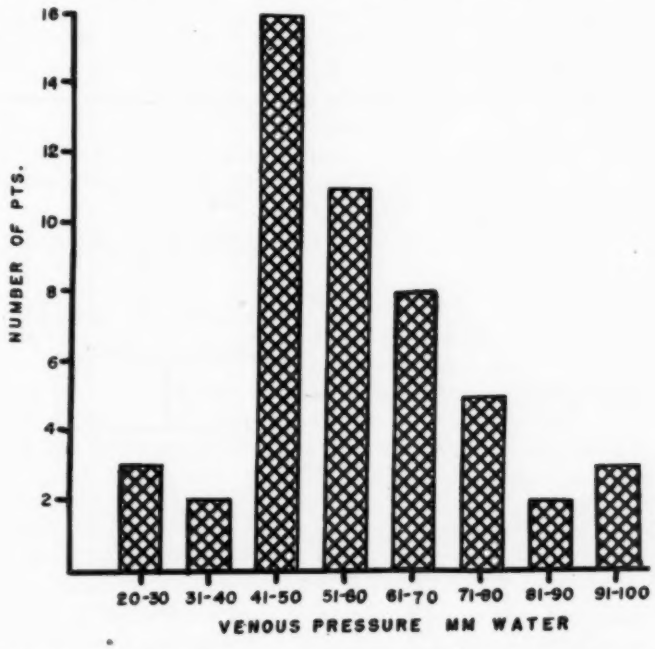

Fig. 1.—The distribution of patients at various venous pressure levels.

RESULTS

Venous Pressures in Normal Children.—The mean venous pressure for fifty children (eighteen girls and thirty-two boys), between the ages of 3 and 10 years, was 54.3 mm. of water with a standard deviation of 17.1. Eighty-six per cent of the group had venous pressures which were between 30 and 81 mm. of water. (Fig. 1.)

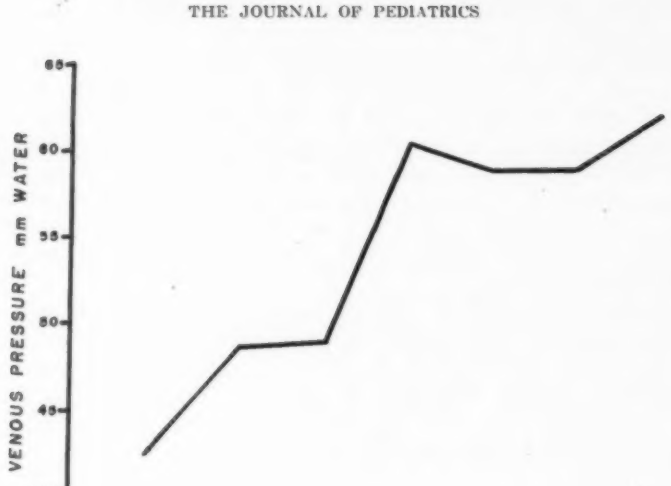

Fig. 2.--The relation of venous pressure to age, using the phlebomanometer and the phlebostatic level as a point of reference.

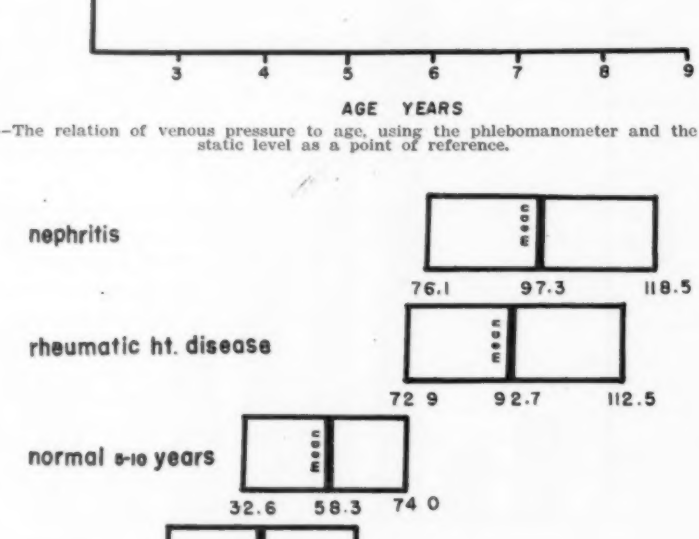

Fig. 3.—Mean venous pressure levels and standard deviations of normal children from 3 to 5 years and from 8 to 10 years of age as compared with the thirteen patients with rheumatic heart disease without clinical evidence of heart failure and the four patients with glomerulonephritis.

Venous pressures in fifty normal subjects between 3 and 10 years of age were analyzed according to age (Fig. 2). The average in the 3-year-old group was 43.3 mm. of water; in the 6-year-old group, 60.5; in the 9-year-old group, 62.1.

Twelve subjects from 3 to 5 years of age had a mean venous pressure of 46.2 mm. of water with a standard deviation of 16.9 (Fig. 3). Thirty-eight subjects (5 to 10 years of age) had a mean pressure of 58.3 mm. of water with a standard deviation of 15.7. In general it can be seen that venous pressure increased with age.

Venous pressures were compared in male and female subjects. The average venous pressure in thirty-two males was 54.9 mm. of water and in eighteen females 53.9. These differences are not significant.

Venous Pressures in Patients With Rheumatic Heart Disease Without Evidence of Congestive Heart Failure.—The antecubital venous pressures in thirteen patients with rheumatic heart disease without clinical signs of congestive heart failure were studied (Table I). Certain patients had evidences of mild or moderate cardiac enlargement or slight abnormalities in the electrocardiogram. The blood pressures were within normal limits. None presented dyspnea, edema, râles, hepatomegaly, or clinical evidence of venous hypertension. The mean venous pressure was 92.7 mm. of water. This may be compared with the mean pressure in normal children of 54.3 mm. of water.

Venous Pressure in Patients With Acute Glomerulonephritis.—Antecubital venous pressures were studied in four patients with glomerulonephritis. Three were in the acute stage with râles and edema. Slight electrocardiographic changes were noted. The average venous pressure for this group was 97.3 mm. of water ± 21.2 (Fig. 3).

DISCUSSION

In 1943 the phlebomanometer was utilized in determining normal venous pressures in adult individuals. The average pressure was 97 mm. of water. This is considerably higher than for individuals between the ages of 3 and 10 years, whose average venous pressure was 54.3 mm. This is in keeping with Hooker's findings of a gradual increase in venous pressure with age.[2] To our knowledge, normal values for venous pressure in individuals below 3 years of age are not known.

In children, as in the adult, there were no significant differences between venous pressures in male and female.

In adult individuals, when the phlebostatic level is used, chest thickness does not materially influence the venous pressure. For example, in adults whose phlebostatic levels averaged 126 mm., the venous pressure was 103 mm. of water; in those whose phlebostatic levels averaged 89 mm., the venous pressure was 104 mm. of water.[3] In children, however, using the same method, the venous pressure increases as the thickness of the chest increases. This may be due to the increase in the venous pressure with age. Children whose phlebostatic levels averaged 60 mm. had venous pressures averaging 40 mm. of water. Those with phlebostatic levels averaging 75 mm., had venous pressures averaging 64 mm. of water.

TABLE I. VENOUS PRESSURES IN THIRTEEN PATIENTS WITH RHEUMATIC HEART DISEASE WHO EXHIBITED NO CLINICAL MANIFESTATIONS OF CONGESTIVE HEART FAILURE

NO.	PATIENT	AGE (YEAR-MONTH)	DIAGNOSIS	A.P. DIAMETER OF CHEST (CM.)	VENOUS PRESSURE	CARDIOTHORACIC RATIO (%)	DIGITALIS	RÁLES	EDEMA	DYSPNEA	BLOOD PRESSURE	ECG FINDINGS
1.	D. J.	5-3	Acute myocarditis	13	55	54	0	0	0	0	95/50	Left axis deviation
2.	P. B.	6-0	Acute myocarditis	16	93	52	0	0	0	0	110/90	Normal axis deviation
3.	B. M.	6-5	Acute myocarditis	16½	91	50	0	0	0	0	110/70	Normal axis deviation
4.	J. L.	6-6	Chronic myocarditis	13½	75	57	0	0	0	0	94/40	Normal axis deviation
5.	Z. A.	6-7	Mitral insufficiency	14½	71	53	0	0	0	0	85/ 0	Slight left axis deviation
6.	L. D.	6-8	Acute myocarditis	14	55	50	0	0	0	0	110/70	Normal axis deviation. P.R. interval 0.17 sec.
7.	N. R.	7-0	Chronic myocarditis	17	75	48	0	0	0	0	100/60	Slight right axis deviation
8.	M. S.	7-6	Mitral insufficiency	16	116	46	0	0	0	0	105/70	Normal axis deviation
9.	D. W.	8-0	Mitral insufficiency	14½	89	51	0	0	0	0	?	Normal axis deviation. P.R. interval 0.16 sec. Wandering pacemaker
10.	R. M.	9-6	Mitral valvulitis	15	107	54	0	0	0	0	125/85	Slight right axis deviation
11.	R. C.	9-9	Mitral insufficiency	15½	108	–	0	0	0	0	115/65	Right axis deviation
12.	L. B.	10-0	Mitral stenosis and insufficiency	15	77	66	0	0	0	0	105/55	Right axis deviation
13.	R. C.	10-8	Mitral stenosis and insufficiency	17	107	42	0	0	0	0	110/70	Normal axis deviation

The direct method was ordinarily a suitable procedure for determining venous pressure in patients 3 years of age or older. In younger patients there was difficulty in securing cooperation. Most accurate venous pressure measurements were determined when the veins were punctured on the first attempt. It was usually accomplished using a No. 25 or 26 needle. Undue trauma caused venospasm and poor cooperation with elevation of the pressure. It should be pointed out that the position of the arm is important. Ideally, the arm was held at approximately 45 degrees from the body. When close to the body, there was often venous obstruction. This likewise occurred when the arm was greater than 90 degrees from the body.

In the above experiments the needle was inserted in the direction of the blood flow. It has been shown that differences in placement of the needle in regard to the direction of the flow produces some differences in pressure. The average difference in the adult was approximately 15 mm. of water. This difference was particularly noticed when small veins were used. Thus in the determination of venous pressure in children, it is essential that the needle be placed in the direction of the blood flow if comparable readings are to be expected.

Venous pressures differ in various veins of the body. Venous pressure is ordinarily higher in veins more distal to the heart. In normal adults, comparative venous pressures are approximately as follows: Antecubital, 97 mm. of water; femoral, dorsal, metacarpal, malleolar, and pedal pressures are 111, 120, 150, and 176 mm. of water, respectively. Thus determinations made in veins other than the antecubital veins require different interpretation. In adults venous pressures in the right and left antecubital veins are essentially the same. It is probable that this also holds true for children. It has been said that the pressure in the veins of the left leg is somewhat higher than that of the right leg. This is allegedly due to the crossing over of the sigmoid and other structures and compression upon the left iliac vein. This, however, has not been confirmed by all observers.

There is a daily variation of venous pressure in the adult, with higher evening readings. This variation may represent a change of as much as 39 mm. of water throughout a twelve-hour period. It is probable that the venous pressures in children undergo the same daily variation. The present venous pressure determinations were made at varying periods during the day, no attempt being made to control this factor. As about half of the venous pressure determinations were made in the evening, the extreme upper limits would include the higher pressures reached. Thus the range of normal is necessarily wide.

Consecutive daily pressures in adults recorded under similar conditions at the same time of the day showed a variation as much as that shown during the course of a single day. It is likely that a similar variation occurs in children. Such daily variations, however, do not invariably occur. In one child in whom venous pressures were determined daily for four days, at different times of the day, the venous pressures were 75, 75, 80, and 58 mm., respectively.

The establishment of normal venous pressure levels in children is essential to the proper classification of many disease states. Venous hypertension, venous normotension, or venous hypotension may exist. In the age group 3 to 10 years,

venous hypertension probably would exist when the antecubital venous pressure is greater than the maximum attained in this series, i.e., 100 mm. of water; and it would possibly exist when the pressure is above 71.4 mm. of water. Venous hypotension would probably exist when the venous pressure is below 24 mm. of water; and it would possibly exist when it is below 37.2 mm. of water. Venous normotension would possibly range between 37.2 and 71.4 mm. of water and probably range between 24 and 100 mm. of water.

Venous hypertension may be either generalized or localized. A generalized increase as detected by multiple venous pressure determinations is caused by right ventricular congestive heart failure; valvular heart disease, especially tricuspid stenosis; congenital cardiac anomalies—for example, congenital tricuspid stenosis; pericarditis, either constrictive or effusive; or following or during intravenous medication, particularly plasma, blood, or serum proteins.

Localized venous hypertension may result from obstructions arising within the vein, i.e., thrombosis or embolism; changes in the vessel wall, i.e., torsion or phlebitis; and changes external to the vessel wall when obstruction is produced, i.e., neoplasia or adhesions.

Venous hypotension is found in patients with shock or peripheral circulatory collapse.

It is possible that the venous pressure is elevated in patients with rheumatic heart disease before other clinical signs of failure are evident. In these patients, many of whom had rheumatic mitral stenosis and/or insufficiency and right axis deviation in the electrocardiogram, there was an increase in the venous pressure. There was, however, no other evidence of congestive heart failure. Large hearts, as measured by the cardiothoracic ratio and as determined fluoroscopically, were sometimes present. It has been said that a large heart is a failing heart. If this is the case, it is probable that an elevated venous pressure is an earlier indication of failure than is edema. It is possible that an elevated venous pressure is the earliest sign of right ventricular congestive heart failure. On occasion, the venous pressure was high when cardiac enlargement was not demonstrable. This may be due to difficulty in demonstrating right ventricular enlargement by x-ray. For example, R.C. (Patient 13) in Table I showed a cardiothoracic ratio of 42 per cent and a venous pressure of 107 mm. of water. The heart in this instance was not clinically enlarged, and the electrocardiogram was within normal limits; however, mitral stenosis and insufficiency were present.

The venous pressure was elevated in four patients with glomerulonephritis. One of these patients showed clinical signs of myocardial damage, but none exhibited clinical evidence of cardiac failure. A high incidence of cardiac involvement is known to occur in this disease.

In congenital heart disease, right axis deviation and right ventricular strain associated with a right auricular strain is a common finding. Not uncommonly an elevated venous pressure is one of the earliest signs of failure of the right side of the heart.

In patients with pericarditis, the venous pressure is often of considerable aid in diagnosis as well as in therapy. A rising venous pressure, particularly when associated with a falling arterial pressure, is ordinarily an indication for surgical intervention.

In the treatment of patients with cardiac disease in whom intravenous therapy, particularly plasma and blood, is administered, venous pressure determinations are highly desirable in controlling the amount and rate of speed of administration. It was noted in one patient with nephrosis, whose resting venous pressure was 54 mm. of water, that the intravenous administration of serum albumin increased the pressure to 69, 97, and 117 mm. of water following the administration of 20, 50, and 75 c.c. of 25 per cent serum albumin, respectively. Thus the administration of 75 c.c. of 25 per cent serum albumin produced an increase of venous pressure which was 100 per cent above the child's normal value.

SUMMARY

The antecubital venous pressure was studied in fifty normal children and in groups of patients with rheumatic heart disease without clinical evidence of congestive heart failure and in patients with glomerulonephritis. The mean venous pressure for normal children between 3 and 10 years of age was 54.3 mm. of water with a standard deviation of 17.1. Between the ages of 3 and 5 years, the mean pressure was 46.2 mm. of water, ± 16.9. Between the ages of 5 and 10 years the mean pressure was 58.3 mm. of water, ± 15.7. The venous pressure increased with age. Patients with rheumatic heart disease without evidence of congestive heart failure and patients with glomerulonephritis had higher venous pressures than did normal individuals. The determination of the presence of venous hypertension, venous normotension, or venous hypotension is of importance, and can be readily ascertained.

We are grateful to Mr. Jack Haverback for the statistical evaluation of this study.

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THE SQUEEZOGRAM: AN OBJECTIVE METHOD FOR RECORDING THE COURSE OF CHOREA

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DURING the past years, many types of therapy have been used for chorea. Some have enjoyed only brief favor;[4] others, such as fever therapy,[1] the ketogenic diet,[2] and phenyl-ethyl-hydantoin (Nirvanol),[3] are currently in use. The evaluation of these various measures has been hampered by the lack of an objective method for recording the severity of the disease and its course during therapy. Although electroencephalography,[5] electromyography,[6] and other technical procedures[7-9] will reveal definite abnormalities in the choreic patient, these methods offer obvious difficulties for routine use. The need for a bedside method of recording the severity of the movements led us to adopt the simple mechanical device described below, which, for want of a better term, we have called the "squeezogram."

PROCEDURES

The apparatus used to record graphically the severity of choreiform and other types of movements is shown diagrammatically in Fig. 1. A small, soft rubber bulb of the asepto syringe type is connected to the tambour by rubber tubing. Changes in pressure on the bulb are transmitted to the tambour. These vibrations are recorded on a smoked drum.

In conducting the test, a horizontal line is drawn on the drum. The needle is adjusted so that it rests about one centimeter below the base line. The patient is instructed to squeeze the bulb so as to bring the needle up to the base line and to maintain it at that level. All distracting factors are removed from the subject's attention, and all recordings are done in a quiet room with only the observer and the patient present. It is emphasized to the patient that he is not competing, merely that a routine record is being made. Remarks are never made regarding poor tracings; and when the subject himself notices increased movements, he is reassured as to their implication.

The subjects of these experiments were patients with chorea on the wards of Bellevue Hospital between July, 1947, and January, 1948. As controls, a number of patients admitted to the Children's Medical Service with diagnoses other than chorea, and a few normal adults were studied with the procedure outlined above.

Under the same general conditions, recordings of other diseases with involuntary movements were obtained. Patients with delirium tremens on the alcoholic wards, and patients with Parkinson's disease in the neurology department were the subjects of these observations.

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EXPERIMENTAL RESULTS

In all the illustrations, the upper tracing of each figure is the left hand, and the lower tracing is the right hand.

Figs. 2, *a* and 2, *b* are examples of tracings of two controls. The first is that of a normal adult; the second that of a patient with rheumatic fever but no chorea. These results were obtained on the first trial. The controls were able to bring the needle up to the base line and keep it on the base line with small variations during the ninety-second revolution of the kymograph drum. The record of a mentally deficient patient is shown in Fig. 2, *c*. His attention

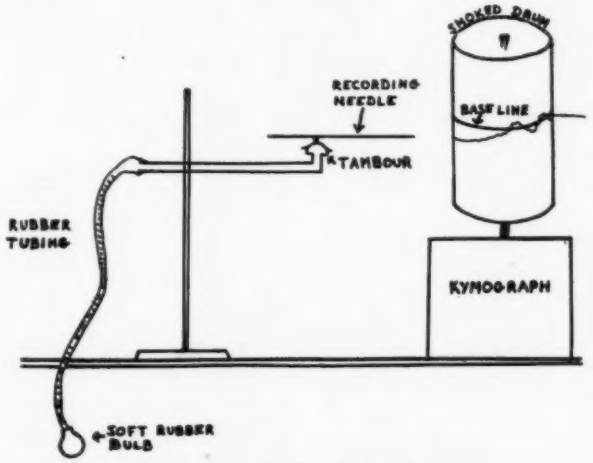


Fig. 1.—Diagram of the apparatus.

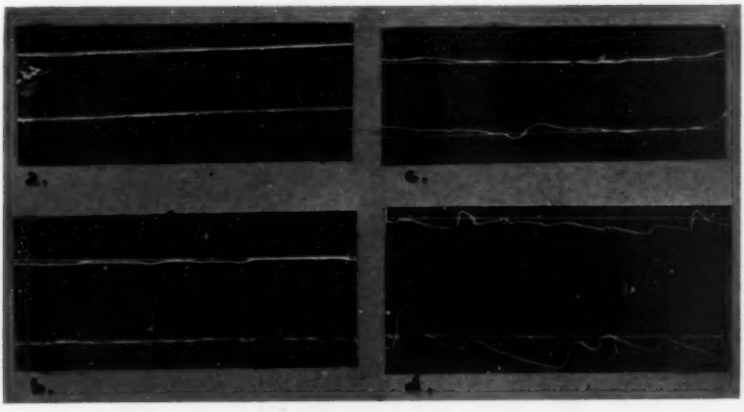
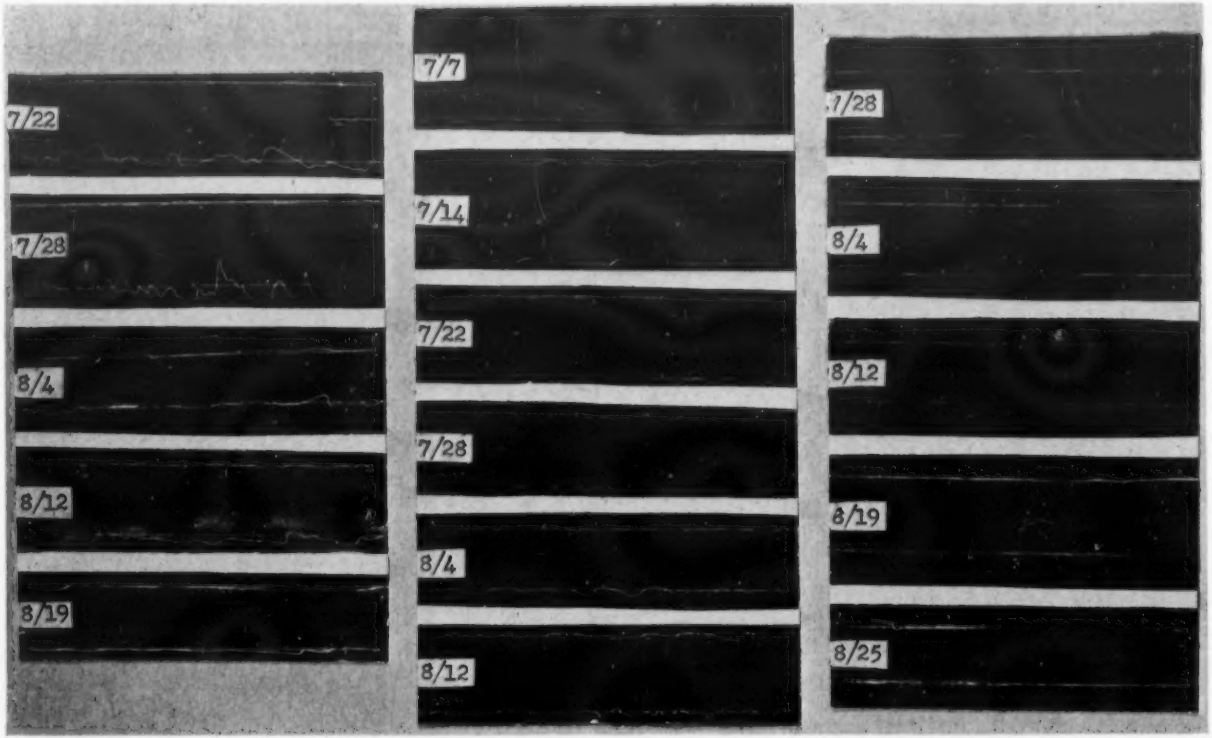


Fig. 2.—The upper tracing in each figure is the left hand, and lower tracing is the right hand. *a*, Normal adult. *b*, Nine-year-old patient with rheumatic fever, but no chorea. *c*, Nine-year-old mental defective patient, unable to cooperate in the test. *d*, Nine-year-old patient with rheumatic fever and active chorea.



a. *b.* *c.*

Fig. 3.—Serial records of patients with chorea. In all figures, the upper tracing is the left hand; the lower tracing is the right hand. *a*, Patient R. B., with hemichorea, demonstrating gradual improvement. *b*, Patient F. S., recording long-standing mild chorea with one relapse (July 28). *c*, Patient M. S., with normal hand tracings although she had choreiform movements of the face.

on the test could not be maintained and he showed irregularities on several attempts. In Fig. 2, *d* a tracing is shown of a choreic patient. The typical irregular movements are well demonstrated here.

Fig. 3 consists of three groups of serial recordings of choreic patients. Some of the patients showing abnormal tracings had two or three tracings taken in a single day. They were compared to determine the influence of practice. No changes were found on recordings taken during a single day.

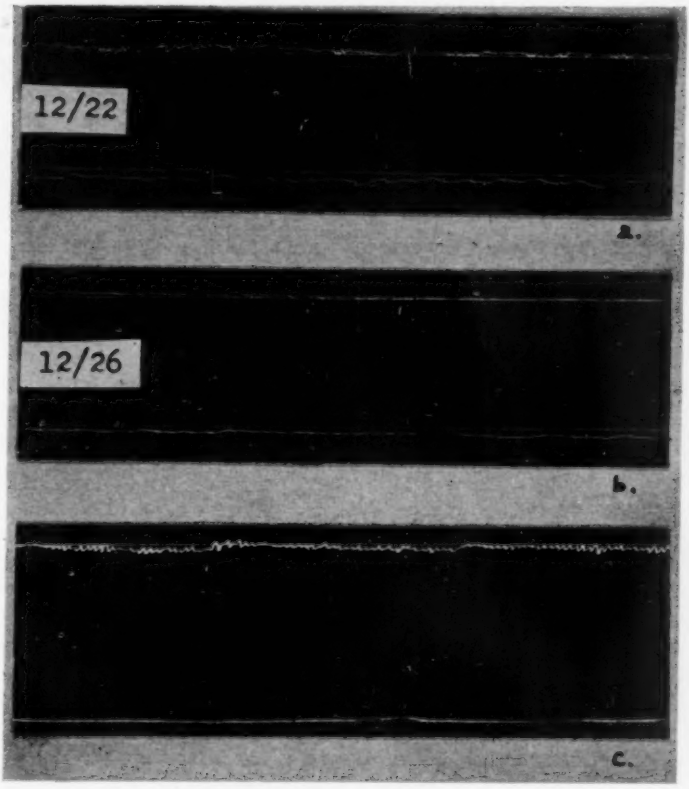


Fig. 4.—Tracings are reproduced in their actual size. In each figure the upper tracing is the left hand, and the lower tracing is the right. *a*, Patient with delirium tremens on admission. *b*, Same patient four days later. *c*, Tracing of patient with Parkinson's disease.

In Fig. 3, *a* are samples of serial recordings of a 5-year-old boy (R. B.) admitted with severe chorea. As is seen in the initial tracing, the left hand was quite normal. The right hand had marked choreiform movements which in subsequent tracings progressed gradually to normal.

Fig. 3, *b* represents recordings from a 9-year-old girl (F. S.) with moderately severe chorea who had been hospitalized for many weeks before observations were begun. The first three tracings reveal a gradual improvement. On

July 28, a temporary relapse is recorded. It was independently agreed that she had become more severe clinically at that time. The patient then went on to a long course of mild chorea.

Fig. 3, *c* shows the tracings of an 11-year-old girl (M. S.) admitted with a two-week history of grimacing, involuntary hand movements, twitching, and loss of coordination. The first recording was taken after she had completed a forty-eight-hour period of starvation and when she had just been started on a ketogenic diet. This shows only an isolated incoordinated movement; but twitching was still seen about the mouth. All the following recordings were quite close to what may be considered normal. In spite of cessation of hand movements, she still manifested choreic movements of her facial muscles and tongue. These latter movements diminished in activity through the first four recording. By the fifth tracing, all clinical signs had disappeared. In this case, the tracings do not represent the true course of her chorea. Such cases must be followed by clinical observation, as no objective technique can be applied easily.

The tracings in Fig. 4 (4, *a* and 4, *b*) are those of a 54-year-old man (B. H.) admitted to the alcoholic ward with delirium tremens. He demonstrated a fine hand tremor superimposed on a coarse tremor of his whole arm. The first record shows this fine hand tremor superimposed on the wavering line. A recording taken four days later (4, *b*), when no fine tremor or coarse tremor of his arm could be demonstrated clinically, showed only a suggestion of tremor.

The tracing of a patient (P. W.) with the tremor of Parkinson's disease is shown in Fig. 4, *c*. Clinically the tremor was very overt in his left hand, while none was noticeable in his right hand. This is borne out by the tracing.

DISCUSSION

The experience which we have had with the squeezogram has shown that it will record objectively the course of chorea. It may, therefore, be applied to evaluating therapeutic procedures. The apparatus is simple and readily available. Frequent records may be easily taken and the results permanently appended to the patient's charts. However, it must be pointed out that this technique is limited by recording only abnormal movements of the hand. This is amply demonstrated by the tracings of Patient M. S. in Fig. 3, *c*. Although she had choreiform movements of the face, her squeezograms were perfectly normal.

It is interesting to note the differences in tracings from other involuntary movements. Those of chorea are coarse, irregular, and uncoordinated. The movements in delirium tremens and Parkinson's disease are fine and regular, and show coordination. The tracings illustrate well what has been noted clinically.

SUMMARY

A simple graphic method for recording the severity of choreiform movements is described. This permits a more exact evaluation of therapeutic agents than has heretofore been possible.

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A GRID FOR RECORDING THE WEIGHT OF PREMATURE INFANTS*

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ALTHOUGH the weight curve of the normal full-term infant is probably as well known as any pediatric dataum, there is surprisingly little information as to the gain in weight of premature infants of various birth weights. The only statistical compilation with which we are familiar is that of Dunham, Jenss, and Christie,[1] who reported a composite weight curve of a group of premature infants between 1,900 and 2,000 Gm. at birth who were followed for twenty days only. It seemed to us highly desirable to have a grid showing the weight expectancy curves of premature infants of various sizes as a standard of reference for their progress, and we accordingly undertook to construct one from data of infants cared for on the Bellevue Hospital premature unit.

The weight curves of 100 premature infants ranging from 1,000 to 2,500 Gm. at birth who had exhibited no untoward complications in the neonatal period were superimposed and "normal" curves were drawn by inspection to conform to the growth patterns so revealed. The accompanying chart (Fig. 1) illustrates the result obtained.

No attempt was made to achieve statistical accuracy in constructing these curves. They do not represent average performance of children on our unit. They represent what the premature infant who develops without complications will do when fed and handled in a certain arbitrary manner, and as such we have found them exceedingly helpful in measuring the progress of our current cases. They are also useful in making comparisons of different foods.

The chief variable in determining the weight curve of such a premature infant is the feeding policy. The routine for the children used in constructing the chart consisted of a regular stepwise increase in the food beginning on the second day of life up to a total of 120 calories per kilogram which was attained on the tenth day of life and was not further increased. Olac was used as the feeding in all instances. We have been interested in comparing these curves with data from two other institutions where a somewhat different feeding routine was followed. The report of Gordon, Levine, and McNamara,[2] from the New York Hospital in which an adequate caloric intake was achieved by the seventh rather than the eleventh day, indicates that a somewhat more rapid increase of weight can be obtained during the first three weeks than we have shown. Conversely, data from a group of premature infants from the Boston Lying-in Hospital analyzed by Clifford and Winter,[3] in which a more conservative early feeding policy was pursued followed by an increase in caloric intake above 120

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*Exhibited at the Fifth International Pediatrics Congress, New York City.

calories per kilogram after the third or fourth week, showed, as might be expected, a less rapid early weight gain and a more rapid one than ours in the later weeks of observation. Although the expected weight gain is, therefore, affected by the caloric intake, the feeding policies employed in this country vary within relatively narrow limits and hence we believe that the weight chart shown will prove useful even under slightly different conditions than those in our clinic.

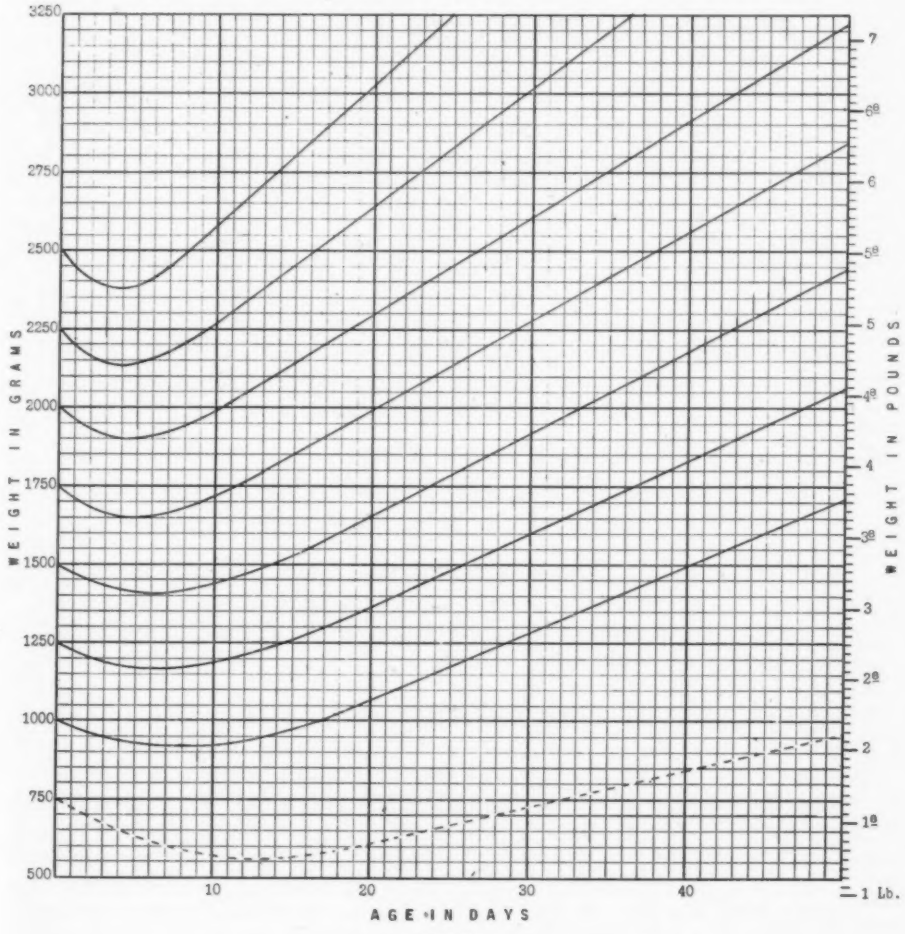

Fig. 1.

In the smallest weight group, below 1,000 Gm. birth weight, we have not found it possible to routinize our feedings and it is often necessary to proceed at a slower rate of increase than that given above. The dotted line shown for

infants weighing 750 Gm. at birth represents observations on a very few infants of this weight who have survived.

SUMMARY

A grid is presented showing expected weight curves for premature infants of varying birth weights. Its usefulness and limitations are discussed.

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EXPERIENCES WITH EPIDEMIC DIARRHEA OF THE NEWBORN

The Use of Nutramigen In Its Dietary Management

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INTRODUCTION

BETWEEN July 26, 1944, and Oct. 10, 1946, a large number of cases of epidemic diarrhea of the newborn appeared in the Philadelphia area. Many of these infants were transferred to the Children's Hospital of Philadelphia for treatment. Here, in spite of careful isolation measures, the infection spread to patients admitted for other disorders. Although not all newly born, many of these secondarily infected infants presented similar clinical courses and showed no parenteral infections. A series of seventy-five patients is studied in this paper, of which sixty-three were admitted from nurseries definitely known to be infected with this disease; the remaining twelve acquired their infections in the Children's Hospital. Only those patients who showed no parenteral infection on admission were included in this series unless it was clearly established that such infection was a complication of a pre-existing diarrhea.

PLAN OF TREATMENT

At the time of admission, most of the infants were believed to be acidotic and the carbon-dioxide combining power was determined in forty-eight cases. Often it was necessary to administer fluid before the sample of blood was withdrawn because of the shocked condition of the patient. Hydration was accomplished first by the intravenous administration of 5 per cent glucose in physiologic saline, followed by the administration of ⅙ molar sodium lactate, the amount of which was adjusted according to the formula of Hartmann and Senn.[1] Half of the sodium lactate was given intravenously and half subcutaneously. In most of the cases this was followed by the intravenous administration of plasma, or, if the infant was anemic, whole blood. In a few cases 5 per cent solution of casein hydrolysate* was given intravenously. During the period of hydration, oral fluids were withheld or greatly restricted, according to the severity of the diarrhea, for periods ranging between 12 and 72 hours, until tolerance to oral feeding was regained. Oral feeding was recommenced in the form of 5 per cent glucose in physiologic saline in small, frequent feedings. If these were well tolerated, the next oral feeding offered was a rice gruel of 5 per cent strength, prepared by long cooking in a double boiler. In some cases other feedings were used in place of the rice gruel; among these were emulsions of dried apple or banana, weak tea, barley water, or farina gruel.

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*Amigen solution, Mead Johnson and Company.

Milk was resumed in some of the patients by using a number of milk products such as casein powder, boiled skimmed milk, skimmed lactic acid milk, and powdered protein milk. In the course of empiric trial, we found that the resumption of milk feeding in the form of Nutramigen* was effective and perhaps better than other types of milk addition.

AN ILLUSTRATIVE CASE

The case of R. D. (45-3457) illustrates the method of treatment with Nutramigen. This infant developed diarrhea in a contaminated nursery, was removed to the Children's Hospital in advanced dehydration and with sclerema. Its weight had fallen from 3,200 Gm. (7 pounds, 2 ounces) to 2,550 Gm. (5 pounds, 10 ounces). Where clyses had been given in the lateral chest walls, the tissue was broken down and suppurating. There were râles in both lungs and the infant appeared feeble and shocked. The diarrhea had begun at age 7 days, the respiratory infection at 10 days. At age 16 days, when admitted, the diarrhea had ceased and the infant had had no stool for forty-eight hours. This was assumed to be due to atonic ileus because the diarrhea returned as soon as intravenous fluid was administered. The plasma carbon-dioxide combining power was 12.5 meq. per liter (28 volumes per cent). This infant was treated intravenously with 5 per cent glucose in physiologic saline, ⅙ molar sodium lactate and plasma for a period of seventy-two hours. At this time 5 per cent rice gruel was given orally and was well tolerated. Five days after admission, 15 Gm. (0.5 ounce) of Nutramigen was added to the daily amount of rice gruel as a test feeding. This was gradually increased by small amounts to a level of caloric adequacy. The child was discharged in healthy condition at the age of 45 days weighing 3,300 Gm. (7 pounds, 4 ounces). The Nutramigen and rice gruel were continued at home. Some time later an attempt was made to replace the Nutramigen with whole homogenized milk. This caused the stools to become loose. The Nutramigen was resumed and the stools again became normal. Shortly afterward, by gradually adding homogenized milk and gradually decreasing the Nutramigen, the transfer was accomplished successfully.

RESULTS

The results in the entire series of seventy-five cases were as follows:

	NUMBER	RATE
Recovered	57	76 per cent
Died	18	24 per cent

The results in the patients fed with Nutramigen were as follows:

	NUMBER	RATE
Recovered	22	95.7 per cent
Died	1	4.3 per cent

FACTORS IN PROGNOSIS

1. *Virulence:* The factor of virulence is difficult of appraisal. Nelson and his co-workers[2, 3] had a much greater mortality rate in their second series than

*Mead Johnson and Company.

in their first. In their first epidemic, in the nursery of a general hospital, only 3.5 per cent died; in their second epidemic in the same institution 23.8 per cent died. The first thirty-seven cases of our series had a mortality rate of 37.8 per cent, while the second thirty-eight cases had a mortality rate of 10.5 per cent.

2. *Interval between onset and admission:* This period was brief in many cases where death occurred and long in many patients who survived. It could not be correlated with the prognosis in this series.

3. *Resumption of milk:* Many infants were found to have recurrences when milk was added to the glucose or rice gruel. In those whose milk was added in the form of Nutramigen, this seemed to occur less frequently. The recovery rate of the patients fed Nutramigen seems better than those fed on other forms of milk. The number of cases is small, and other factors, such as lower virulence, may be partly responsible for the better results.

4. *Relapses:* These occurred in thirty-six of our seventy-five patients, or 48 per cent. They have been referred to as the "biphasic course" in other papers. Of the thirty-six infants who had relapses, ten died, or 27.7 per cent, little above the mortality rate of the group as a whole (24 per cent).

5. *Severity of the acidosis:* In forty-eight infants the plasma carbon-dioxide combining power was determined before fluid was administered. The results in these infants were as follows:

ADMISSION PLASMA CO_2	RECOVERED	DIED
Less than 9 meq./L. (20 volumes per cent)	10	3
Between 9 meq./L. and 13 meq./L. (20 to 30 volumes per cent)	7	6
Over 13 meq./L. (30 volumes per cent)	18	4

From these data it is impossible to make any correlation between the severity of the acidosis and the prognosis.

6. *Birth weight*: In an attempt to determine whether or not the larger infants had a better chance of recovery, the following data were collected:

BIRTH WEIGHT	RECOVERED		DIED	
	NUMBER	PER CENT	NUMBER	PER CENT
Under 2,500 Gm. (5 lb. 8 oz.)	3	27.3	8	72.7
Between 2,500-3,200 Gm. (5 lb. 8 oz.-7 lb.)	30	82.3	6	16.7
Over 3,200 Gm. (7 lb.)	19	90.5	2	9.5

A definitely lower mortality is seen in the infants of greater birth weight and a very poor prognosis can be assumed from the data of the infants weighing less than 2,500 Gm. (5 pounds 8 ounces) at birth.

7. *Extent of the weight loss before admission:* The difference between the birth weight and the admission weight was ascertained in sixty-four cases. In some infants there had been substantial gains of weight before the diarrhea began: in spite of great losses of weight, some of these infants were still above birth weight. In most cases the maximum weights were not available; as most of them were newborn the maximum weight must have been near the birth weight. The following results were obtained in sixty cases:

	RECOVERED		DIED	
	NUMBER	RATE (PER CENT)	NUMBER	RATE (PER CENT)
Patients over birth weight	6	85.7	1	14.3
Patients at birth weight	5	50.0	5	50.0
Patients having lost 15 per cent or less	18	77.4	5	12.6
Patients having lost 16 per cent to 30 per cent	16	80.0	4	20.0

The five infants admitted at birth weight who died were all very small infants weighing respectively 908, 1,360, 1,360, 1,816 and 2,540 Gm. (2, 3, 3, 4, and 5.6 pounds). None had lost any weight when the diarrhea began.

There seems to be no correlation between loss of weight and mortality in this series.

DISCUSSION

We have attempted to predict the course of our cases by some measurable characteristic. The duration of the diarrhea prior to admission was not significant. In some cases active replacement therapy might have been delayed too long. In others a long pretreatment period might indicate that the infection was of low virulence or that the infant had or could develop ability to resist the infection. In the severest cases death occurs after a very brief period of illness and the disease is often not controlled by the accepted forms of treatment.

The occurrence of relapses did not appear to be significant in prognosis, as nearly three-fourths of the patients having these survived.

The severity of the acidosis appeared to reflect the amount of water loss rather than the virulence of the infection. Most of the infants with severe acidosis recovered. The severity of the weight loss, likewise reflecting the amount of water loss, cannot be correlated with the prognosis.

However, it seems very clear that small size at birth is a factor which makes the prognosis much more grave. However, Glynn[4] reported 83 per cent of recoveries in his premature infants. Our poor results with these may reflect lack of facilities in the institutions referring these infants and the factor of exposure in transfer.

We are interested in the relation of resumption of milk feedings to the prognosis in these cases. Our data for infants whose milk feeding was resumed with Nutramigen were more favorable than those for the group as a whole. Inspection of the records shows that these infants were on the whole larger than those who did not receive it. Many of the Nutramigen fed infants were obviously very severely affected as judged by clinical appraisal. No clinical tetany has appeared in the postacidotic stage of these infants' cases: this may be due to the fact that Nutramigen contains a liberal amount of calcium gluconate (3.5 per cent). We have made no chemical determinations of the serum calcium, however, in these patients, to lend support to such a surmise.

It is our opinion that the Nutramigen should be continued in these cases until the danger of relapse is well past and that the Nutramigen should be re-

placed by milk in a gradual manner. We have seen not a few instances in which an abrupt change caused the diarrhea to recur.

SUMMARY

1. Seventy-five cases of epidemic diarrhea of the newborn were observed and treated during the period from July 26, 1944 to October 10, 1946. Twelve of these cases were acquired in the wards of our hospital from other patients infected with the disease. Some of this twelve were past the newborn period.

2. Hydration and correction of the acidosis were accomplished by intravenous and subcutaneous therapy with glucose, saline, and sodium lactate.

3. Oral feeding was commenced with small feedings of 5 per cent glucose in physiologic saline, followed by the feeding of a 5 per cent rice gruel.

4. Nutramigen was used as a beginning milk feeding in twenty-three cases, either with 5 per cent rice gruel or with boiled water.

5. The total mortality of the series was 24 per cent. The mortality of the cases fed with Nutramigen was 4.3 per cent.

6. Patients with relapsing or "biphasic" courses did not have an appreciably higher mortality than that of the series as a whole. Likewise, the severity of the acidosis at the time of admission had no direct bearing on the prognosis.

7. Low birth weight had a very definite influence in increasing the mortality.

8. We feel that Nutramigen is a very useful substance with which to resume the feeding of milk.

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THE TREATMENT OF ACUTE HEMATOGENOUS OSTEOMYELITIS OF THE LONG BONES IN INFANTS AND CHILDREN

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DURING the past few years the treatment of acute hematogenous osteomyelitis has so changed that the management of this disease presents a problem which now is essentially medical rather than surgical. Thus, the pediatrician is now called upon to treat patients with osteomyelitis by coordinating the surgical, antibiotic, chemotherapeutic, and supportive measures to be employed. A review of the literature reveals relatively few reports on the treatment of osteomyelitis with penicillin, some of which are listed in the bibliography of this paper. Only one of these reports is published in a pediatric journal; namely, the report of Greengard[1] which deals with a general discussion and the treatment of acute hematogenous osteomyelitis in infancy. It is felt, therefore, that the report of some observations on the treatment of seven consecutive cases of acute osteomyelitis of the long bones in infants and children may be of value.

CASE REPORTS OF INFANTS

CASE 1.—R. T., a 5-month-old Negro male infant, was admitted to the Gallinger Municipal Hospital on Jan. 14, 1946, because of fever and paralysis of the right arm.

This patient had a history of a mild cold starting about two weeks before entry. Six days before admission it was noted that he had pain on movement of the right arm, and it seemed as though this arm were partially paralyzed. Fever was noted for approximately one day before admission to the hospital.

Physical Examination.—Temperature was 104° F., rectally on admission. The examination was normal with the exception of the right arm. It was noted that there was no voluntary movement of this arm and that passive movement caused pain. The right shoulder was moderately swollen and a fullness of the axilla was noted.

Laboratory Data.—Two blood cultures, a blood Kahn, and a tuberculin patch test, were negative. A blood count showed 10,600 leucocytes with 84 per cent polymorphonuclears and 16 per cent lymphocytes, and 9.5 Gm. of hemoglobin. Roentgenograms of the right humerus and clavicle were negative at the time of admission.

Course.—Penicillin, 20,000 units every three hours, was started on the day of admission. The temperature continued to be constantly elevated for four days and was of a septic type for two and one-half days more before

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returning to normal. Pain in the right shoulder area disappeared after five days of treament, and swelling resolved by the sixteenth hospital day. Repeat roentgenograms on the fifteenth hospital day revealed a circumscribed area of bony resorption, 1 cm. in diameter, at the metaphyseal end of the right humerus. Penicillin was discontinued on the nineteenth day. The patient was discharged in good condition after twenty-two days in the hospital. During the twenty-two months following discharge the infant had no further difficulty with the right arm. Follow-up x-ray examinations one week after discharge showed a circumscribed area of bone resorption similar to that seen two weeks earlier. Roentgenograms twenty-two months after discharge showed the right humerus to be normal.

CASE 2.—C. S., a 1-month-old Negro male infant, was admitted to the Gallinger Municipal Hospital on Oct. 4, 1946, because of swelling of the right leg of one day's duration.

One day before admission there was swelling of the right knee and lower two-thirds of the right thigh. This area was painful to touch. It was noted that the infant did not move the right leg for the twenty-four-hour period before admission. The family history was negative with the exception that the mother had been given a fifteen-day course of penicillin for the treatment of syphilis in the third month of pregnancy.

Physical Examination.—The temperature was normal on admission. The examination was normal with the exception of the right extremity. The right knee and lower thigh were moderately swollen, tender, and painful on motion. This thigh and knee were slightly warmer than the rest of the body.

Laboratory Data.—Hemogram showed 10,000 white blood cells of which 28 per cent were polymorphonuclears, 8 per cent eosinophiles, 1 per cent basophiles, 7 per cent monocytes, and 56 per cent lymphocytes. Three blood Kahn examinations were negative. On the first hospital day roentgenograms of the right femur were negative. (Fig. 1.)

Course.—A tentative diagnosis of acute osteomyelitis was made on admission. The patient was treated with 15,000 units of penicillin every three hours for ten days, a total of 1,200,000 units. There was no fever during the period of hospitalization. Three days after the beginning of treatment the infant could move his right leg. The redness and swelling of this leg gradually disappeared. X-rays taken at the end of treatment, on the fourteenth hospital day, showed destruction of the end of the right femur, with slight rarefaction of the shaft and a moderate amount of periostitis. Repeat films taken on the twenty-fifth hospital day and again one and one-half months after discharge showed definite healing. The patient's course from the time of discharge until the last clinic visit on Dec. 5, 1947 (a period of fifteen months) has been uneventful, and the infant has acted normally in all respects. X-ray examinations at eight and fifteen months after the onset of this disease showed the right femur to be normal in appearance. (Fig. 1.)

Fig. 1.—X-rays of the right femur, Case 2. *A*, Normal bone on admission. *B*, On the fourteenth day there was considerable destruction at the lower end of the femur with slight rarefaction of the shaft and moderate periostitis. *C*, On the twenty-fifth day there is definite healing. *D*, and *E*, One and one-half and fifteen months after onset. The bone is normal.

CASE REPORTS OF CHILDREN

CASE 3.—E. P., a 6-year-old Negro male child, was admitted to the Gallinger Municipal Hospital on Jan. 2, 1945, because of painful, swollen left ankle.

This patient began to complain of pain in the left ankle three days before entry. At about this time it was noted that the left ankle was swollen and tender to touch. The patient's mother felt that he had fever for two days before admission to the hospital.

Physical Examination.—The temperature on admission was 104° F. (rectally). The examination was normal except for a moderate swelling, extreme tenderness, and pain over the left ankle.

Laboratory Data.—A blood culture, blood Kahn, and a tuberculin patch test were negative. The hemogram showed 58 per cent hemoglobin with 10,700 leucocytes per cubic millimeter. Roentgenograms of the left ankle area on the first hospital day were negative. On re-examination of this angle on the ninth hospital day, x-ray revealed a periostitis of the medial border of the lower one-third of the left tibia.

Course.—Sulfadiazine, 130 mg. per kilogram, and penicillin, 20,000 units every two hours, were started, respectively, on the day of admission and on the second hospital day. Under this treatment the swelling and pain gradually subsided so that by the eighth hospital day these findings were absent. Fever continued for the first four days in the hospital. The temperature then returned to normal. Penicillin dosage was reduced to 10,000 units every two hours on the sixth hospital day and continued for a total of twenty-three days. On the twelfth day after admission the temperature rose to 105° F. (rectally) and remained elevated for two days until sulfadiazine was discontinued. It was felt that the rise in fever probably was due to sulfadiazine sensitivity, but the subsequent administration of sulfadiazine from the twenty-first hospital day through the twenty-eighth day caused no rise in fever. On the nineteenth day after admission, and again on the thirty-eighth hospital day, x-rays revealed some increase in the previous periostitis with slight rarefaction of the distal end of the left tibia. The patient was discharged in good condition on the forty-fifth hospital day.

He was doing well when seen in the outpatient clinic one month after discharge. A repeat x-ray thirty-eight days after his release from the hospital (twelve weeks after onset) showed almost complete healing of the previously described osteitis and periostitis. The patient has moved from the city and has not been seen since the date of the last mentioned x-ray (April 6, 1945).

Case 4.—M. J., a 7-year-old Negro girl, was admitted to the Gallinger Municipal Hospital on Feb. 7, 1945, because of pain in the right shoulder of two days' duration. The patient was perfectly well until two days before entry when she developed a pain in the right shoulder and, at about the same time, felt feverish. Swelling of the right shoulder was first noted on the day before admission.

Physical Examination.—The temperature was 102° F. (rectally) upon admission. The remainder of the examination was normal except for pain and moderate swelling over the right clavicle.

Laboratory Data.—A blood culture revealed the presence of *Staphylococcus albus* and *aureus.* A blood Kahn and a tuberculin patch test were negative. The blood count showed 11 Gm. hemoglobin per 100 c.c., and 25,000 leucocytes per cubic millimeter. On the tenth hospital day x-ray of the right clavicle showed no pathology. (Fig. 2.)

Course.—Sulfadiazine and penicillin, in dosage of 130 mg. per kilogram and 200,000 units per day by intramuscular drip, were started, respectively, on the day of admission and on the second hospital day. Under this treatment the fever ran a continued course for five days before returning to normal. The pain gradually lessened each day until by the seventh hospital day it had completely disappeared. Sulfadiazine was administered for fourteen days and then discontinued. Two weeks after entry 20 c.c. of pus were aspirated from a soft fluctuant mass that had appeared over the right clavicle. On the twenty-second hospital day the distal end of the right clavicle showed rarefaction and irregularity in its outline. On the thirty-fifth day after admission x-ray showed the presence of sequestra and some increased rarefaction. Penicillin was continued for twenty-seven days; the dosage being reduced, during the last week of its administration, to 5,000 units every three hours. The child was discharged in good condition on March 26, 1945, six weeks after entry.

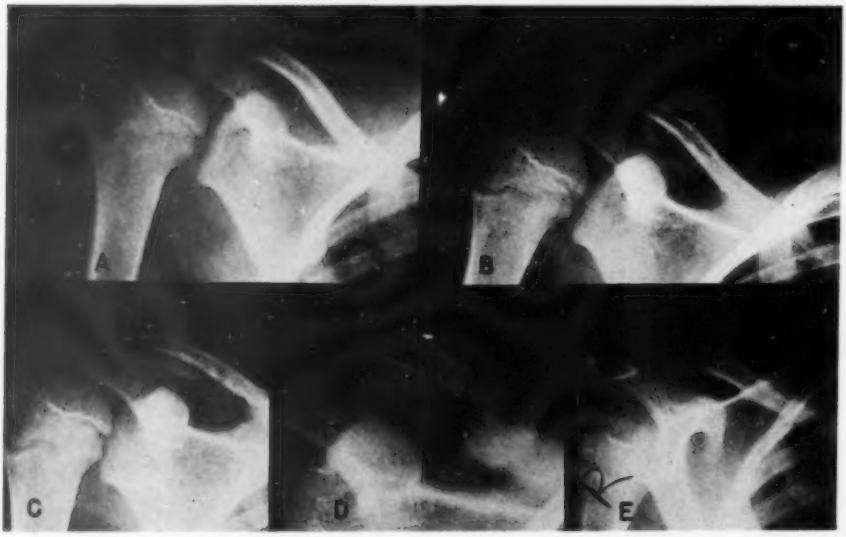

Fig. 2.—X-rays of the right clavicle, Case 4. *A*, On the tenth hospital day the bone was normal. *B*, On the thirty-fifth day after admission there was diffuse rarefaction of the bone with some sequestration. *C*, Two months after admission there was continued increase in the bony destruction. *D*, Four months after entry there was some healing but a pathologic fracture was present. *E*, Thirty-three months after discharge the clavicle was essentially normal.

The patient was seen in the clinic on April 8, 1945, at which time there was continued increase in the bony destruction in the right clavicle. No further treatment was given and when she returned on June 11, 1945, four months after onset, the inflammatory lesion showed some healing, but there was a pathologic fracture at the site of the osteomyelitis.

The patient did not return for the treatment of this lesion, nor did she attend other clinics in the city. An examination in December, 1947, however, revealed that the patient had had no further difficulty since she was last seen,

and that there was no palpable difference between the right and left clavicles. X-ray examination thirty-three months after discharge (Dec. 16, 1947) showed the clavicle to be essentially normal, with no evidence of active bone disease.

CASE 5.—C. E., an 8-year-old Negro boy, was admitted to the Gallinger Municipal Hospital on March 9, 1945, because of pain in the left knee of one day's duration.

The patient had an upper respiratory infection for one week before entry with a fever as high as 103° F. during this interval. Two days before admission he struck his left knee with a piece of tin, and on the following day he noted that the left knee was painful. Pain in the knee remained until admission on March 9, 1945. The past history revealed a previous bout of acute osteomyelitis in the same site in June, 1943, which had resolved without surgery following the use of staphylococcus antitoxin and sulfathiazole.

Physical Examination.—The temperature was 102° F. (rectally). The examination was otherwise normal with the exception of the lower portion of the left thigh, which was moderately swollen. Within this swollen area an extremely tender, small fluctuant mass was noted over the medial condyle of the left femur.

Laboratory Data.—Blood cultures were twice negative. A hemogram showed 13,400 leucocytes per cubic millimeter. The blood Kahn was negative. On the first hospital day x-ray of the left femur was negative.

Course.—Penicillin, in dosage of 10,000 units every two hours, and sulfadiazine were started on the day of admission. The temperature returned to normal after five days. Tenderness, pain, and swelling of the left lower thigh gradually lessened until all were absent on the eleventh hospital day. On the seventh hospital day a large area of rarefaction was noted in the distal metaphyseal end of the left femur. The same findings were present on repeat films made on the fifteenth day after admission. Sulfadiazine and penicillin were discontinued on the eighth and fifteenth hospital days, respectively. The patient was discharged with no complaints and with a negative physical examination on March 31, 1945, twenty-two days after admission.

This patient failed to return to the outpatient clinic as requested, but a re-examination in December, 1947, showed that he was perfectly well since discharge. X-ray examination thirty-three months after discharge (Dec. 11, 1947) showed the left femur to be entirely normal.

CASE 6.—P. B., a 4-year-old white boy, was admitted to the Gallinger Municipal Hospital on Dec. 7, 1946, because of vomiting and pain in the right leg.

Two days before entry it was noted that this child began to complain of pain in the right leg with inability to walk. Vomiting was also noted on this date. On the following day the fever became apparent.

Physical Examination.—The temperature was 104.8° F. The physical examination was essentially normal with the exception of the skin and the right leg. A few scattered petechiae were noted over the chest. The lower one-

half of the right thigh was moderately swollen and extremely tender to palpation. This area was also warmer than the rest of the body. Examination of the lower one-half of the right thigh gave the impression that a deep cellulitis might have existed because of a hard area deep in the central portion of the zone of tenderness and warmth.

Laboratory Data.—A blood culture revealed *Staph. aureus* to be present. The blood count showed 70 per cent hemoglobin with 14,650 leucocytes per cubic millimeter on admission. On the fourth hospital day roentgenograms of the right femur were negative.

Course.—Penicillin and sulfadiazine were started on the day of admission. Penicillin was given in doses of 20,000 units every three hours for one day and was then increased to 50,000 units every three hours. Sulfadiazine was given in dosage of 130 mg. per kilo per day. The temperature continued to be elevated for the first nine days' stay in the hospital, but from that time until discharge was normal. Penicillin and sulfadiazine were continued for the first twenty-three days after admission. The lower portion of the right thigh became somewhat fluctuant on the sixth day after treatment. Thereafter the swelling of the right femur gradually subsided until at the time of discharge, on the twenty-seventh hospital day, the swelling was almost absent. X-rays at this time showed definite periostitis and small areas of bone destruction in the distal metaphysis of the right femur. These changes were thought to be the nomal evolution of a disease process controlled by penicillin.[4]

The patient had no complaints when seen on his first outpatient visit two weeks after discharge, and at this time the x-ray examination revealed increased periosteal reaction and increased osteitis at the distal metaphysis of the femur. This also was thought to be compatible with the normal resolution of the lesion. The patient did not return to the clinic again until March 28, 1947, almost four months after onset, when he was readmitted to the hospital because of pain in his right thigh. The history given at the time of the second admission revealed that the patient had done well until five days before the second admission when his right thigh was squeezed. From the time of this incident until he was readmitted on March 28, the patient had complained of pain in the right thigh. He had begun to walk with a limp. Examination at this time revealed moderate swelling and tenderness, particularly of the anterior and lateral aspects of the right thigh. The patient had a leucocyte count of 14,250 of which 74 per cent were polymorphonuclears, 24 per cent were lymphocytes, and 4 per cent were eosinophiles. A blood culture was negative. X-ray examination on the day of the second admission (March 28, 1947) showed marked periosteal thickening and both productive and destructive bone changes in the distal shaft of the right femur. Sequestra were also noted in this area.

Therapy during this second admission consisted of 50,000 units of penicillin every three hours for the first thirty-four days in the hospital. The course during this period of penicillin therapy, and until the forty-eighth hospital day (May 16, 1947) was uneventful. On this day he struck his right leg against the side of the crib with resultant pathologic fracture of the right femur. A

plaster spica was applied on the day following this fracture. The patient was discharged in a cast after sixty-one days in the hospital. After discharge following this second admission the patient has been seen in the outpatient clinic. His progress was satisfactory and by Aug. 27, 1947, he was walking without crutches. On this date a slight limp and slight muscle atrophy were noted on physical examination. He was seen again on Feb. 2, 1948. Repeat x-ray films made at that time showed anterolateral bowing at the site of the pathologic fracture, with marked sclerosis of the middle third of the bone. There was no evidence of active bone disease.

CASE 7.—H. D., a 7-year-old Negro boy, was admitted to the Gallinger Municipal Hospital on Aug. 16, 1947, because of pain in the left leg and fever of two days' duration. Three days before admission this patient struck his left leg on a step. Fever, swelling, and onset of pain in the left leg were noted two days before entry. These symptoms gradually increased in intensity until the time of admission.

Physical Examination.—The temperature was 102° F. (rectally). Examination was normal except for the lower left leg where, just proximal to the medial malleolus, a tender, warm, swollen area was noted.

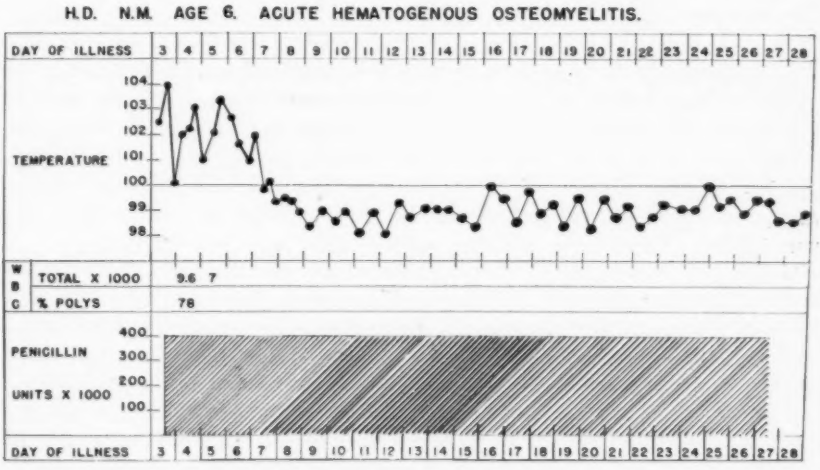

Fig. 3.—The clinical chart of H. D., Case 7.

Laboratory Data.—A blood Kahn was negative. The blood leucocytes numbered 8,600 with 80 per cent polymorphonuclear leucocytes, 18 per cent lymphocytes, and 2 per cent monocytes. The sedimentation rate was normal. Blood culture on two occasions was contaminated. A tuberculin patch test was negative. Roentgenograms of the left lower leg were negative on the second hospital day.

Course.—Penicillin was started on the day of admission in dosage of 50,000 units every three hours. Under this treatment the temperature remained elevated

between 100° and 104° F. (rectally) until the fourth hospital day, at which time it returned to normal. (Fig. 3.) Tenderness and pain of the lower left leg had almost disappeared by the third hospital day. The remainder of the course was uneventful. On the twentieth hospital day roentgenogram of the left tibia showed slight periostitis and some osteitis. Penicillin was discontinued after having been administered for twenty-four days. The patient was discharged completely asymptomatic on Sept. 12, 1947, twenty-seven days after entry.

The course after discharge was uneventful. No pain, tenderness, or swelling were noted after the patient left the hospital. X-ray follow-up studies on the eleventh day after discharge showed some recalcification of the previous area of osteitis at the distal metaphyseal end of the tibia. Walking was permitted at about this time. X-rays one and two months after discharge showed complete healing and disappearance of the osteitis and periostitis previously described. Five and one-half months after discharge there was a mottled appearance at the metaphyseal end of the left tibia, thought to be due to a sclerosis. Eight months after onset re-examination of the left ankle showed almost a complete clearing of the bone changes previously described in the distal end of the tibia. There was at that time no definite evidence of active bone disease.

DISCUSSION

The results of treatment with penicillin and sulfadiazine in acute hematogenous osteomyelitis in infants (both of our infant patients were less than 6 months of age) and in children are not comparable because of the natural difference in the course of this disease in these age groups. Green and Shannon,[3] in their series of infants under 6 months, report a 44 per cent mortality rate. However, in those infants with acute osteomyelitis who survived, fairly rapid healing and eventual complete resolution of the bone was the rule, while sequestration and chronic draining osteomyelitis occurred infrequently. A quite different course occurs in chemotherapeutically and antibiotically untreated acute hematogenous osteomyelitis in young children. Green,[2] and Green and Shannon[3] point out that this is due to differences in the osteolytic power of the usual infecting organism (a streptococcus occurs in 63 per cent of cases in infancy, and *Staph. aureus* occurs in 91 per cent of cases in children)[2]; the thinner, more vascular and spongier texture of the cortex of the infant's long bones; and lastly, because of the more loosely attached periosteum in infancy. In infants, all this favors the rupture of the bone abscess into the subperiosteal space and then, in turn, into the soft tissues.

The course of the two infants in our series shows the rapid resolution of the disease under penicillin therapy in dosage of 20,000 units every three hours for nineteen days in one instance, and a dosage of 15,000 units every three hours for ten days in the other case.

In the childhood group, four of the five patients had sulfadiazine in combination with penicillin. The dosage of penicillin was smaller (10,000 to 25,000 units every three hours) in the cases treated in 1945 than the dosage we now feel is optimal for the treatment of this disease. This was so largely because of

the difficulty of securing this drug. As can be seen, good results were obtained in all cases but one; namely, Case 6, (P. B.) in whom, in retrospect, it is felt that aspiration or open surgical drainage probably should have been carried out to evacuate the subperiosteal abscess. More prolonged administration of penicillin well may have benefited this patient also. The other cases required no surgical treatment of any nature with the exception of Case 4 (M. J.), in whom one aspiration of 20 c.c. of pus was made, and on whom no further procedures were employed, though immobilization of her fracture certainly was indicated.

These results, we feel, were in a good measure possible because penicillin therapy alone or in combination with sulfadiazine was started early in the course of the disease in all patients. Thus, it is essential that the doctor who is responsible for the care of infants and children have, at all times, a high degree of suspicion for the presence of this disease. For this reason we are giving a brief outline of the diagnostic points and conditions to be differentiated: All infants or children who are presented with the picture of pain, protective movements of an extremity, heat and swelling of the painful extremity, and localized tenderness of such areas should be investigated carefully for the presence of acute hematogenous osteomyelitis. The diagnosis is primarly a clinical one for, as is well known, bone changes visible by x-ray do not occur for at least seven to fourteen days. If this interval for bone changes is awaited before therapy is started, the period of medical treatment will have escaped and the condition will be one in which surgical intervention will be almost inevitable. Conditions that must be considered and differentiated from acute osteomyelitis are acute arthritis, cellulitis, scurvy, syphilis, thrombophlebitis, poliomyelitis, and rheumatic fever. If these conditions cannot be differentiated conclusively from osteomyelitis, it is preferable that they be treated unnecessarily with penicillin, rather than that possible osteomyelitis go untreated.

TREATMENT

The excellent results obtained in six of these seven cases reported, and the experiences of Altemeier,[4] Altemeier and Helmsworth,[5] McCorkle, Silvani, Stern and Warmer,[6] and Compere, Schnute, and Cattell[8] show that surgery can be avoided, mortality lowered to almost the vanishing point, and the patient adequately treated by medical means.

Altemeier[4] and Altemeier and Helmsworth,[5] in their excellent articles on this subject, have shown that the results of penicillin therapy are dependent upon early adequate treatment. It can be stated generally that the amount of bone destruction and the necessity for surgery are related directly to the number of days' delay in instituting penicillin therapy. Other factors to be considered, however, are the virulence and sensitivity of the organism, the extent of area involved, the adequacy of therapy, and the age of the patient. Altemeier and Helmsworth[5] have reported the following time relationship to treatment and results: If treatment is begun within the first two to three days of illness, prompt recovery usually results without resort to surgery. Rarely, under these circumstances, will a small subperiosteal or deep abscess require drainage. (Our

Cases 4 and 6 are examples of the exceptions.) If proper therapy is delayed to between four and seven days from the time of onset, the likelihood of surgical drainage (aspiration or incision) is increased and sequestration occasionally develops. Delay beyond seven days usually results in marked bone destruction, requiring not only medical therapy but also major surgery for drainage of abscesses and removal of sequestra.

It is evident that the best results in treating acute hematogenous osteomyelitis are obtained in those cases in which treatment is started during the first two to three days of the disease. Thus, in order to avoid delay, treatment should be initiated even when the diagnosis may be somewhat in doubt. This therapy should be continued until acute osteomyelitis is ruled out as a diagnostic possibility. Examples of such a situation are the several cases of deep cellulitis in which we could not completely eliminate osteomyelitis as a diagnostic possibility, and in which penicillin was continued until the clinical course and x-ray studies pointed to the absence of bone infection. We have seen at least one case in which another possibility exists; the clinical course was typical of acute osteomyelitis but x-ray changes never occurred to confirm the diagnosis. It is possible that early therapy so limited the gross bony changes that they were not extensive enough to be seen by x-ray. Similar experience has been noted by Higgins, Browne, and Bodian[9] and Altemeier and Helmsworth.[5]

The use of sulfonamides in the treatment of acute osteomyelitis has been of considerable value, but the addition of penicillin to our therapeutic armamentarium has greatly improved the prognosis of this disease. Mathews and Hutter[10] have reported the results of sixteen cases of acute osteomyelitis treated with sulfonamides as compared to nine cases treated with penicillin and sulfonamide. They gained the definite impression that the penicillin-sulfonamide series had the least severe bone lesions. It was noted that 90 per cent of the sulfonamide series had surgical intervention as compared to but 20 per cent (two patients required aspiration) in the penicillin group. The majority of our patients had sulfadiazine and penicillin, but we now feel that penicillin alone in adequate dosage probably will be sufficient. We have no definite evidence to show that sulfadiazine has not added to the effectiveness of the therapy. However, the results of others[4, 5, 6] and the results with three of our patients show that penicillin alone, when used early, is an excellent agent for the treatment of acute osteomyelitis.

The dosage of penicillin to be used in the treatment of acute hematogenous osteomyelitis in infants and children is very important. Reasonably good results have been obtained when doses varying from 10,000 to 24,000 units every two or three hours have been employed. Surgical intervention has been necessary in several patients who have been treated with this dosage schedule, however,[6, 7] and it is our impression that with these doses, the course has been more protracted than might be necessary. In order to attempt to reduce the occasions for surgery and to speed up the recovery, we are now using a dosage schedule of 50,000 units of penicillin every three hours for from two to four weeks or more. We feel that penicillin in maximal doses should be given for at least two

weeks and never less than one week after the temperature is normal and the symptoms have subsided. If the infection seems to be severe and bone destruction appears to be extensive, the administration of penicillin probably should be continued for longer periods, even up to four or six weeks. We are not certain that infants require as heavy dosage of penicillin as do older children, but we have gained the clinical impression that infants require almost equal amounts of the drug as do older children or young adults in the treatment of the same disease.

Based upon our experiences with these seven cases of this disease, and upon a review of available literature, we are now using the following general plan for care of acute osteomyelitis. This plan has been developed as we have gained experience with the "medical handling" of this disease and as penicillin has become more available.

1. The treatment of osteomyelitis is started in all cases at the earliest possible moment when a tentative diagnosis is made, or when some other diagnosis, such as cellulitis, seems likely but osteomyelitis cannot be ruled out completely.

2. Supportive care for dehydration and pain, and other symptomatic therapy are given as the condition may indicate.

3. Penicillin is administered in dosage of 50,000 units every three hours intramuscularly for fourteen to twenty-eight days or more.

4. Orthopedic consultation is obtained in all cases, but generally the care is chiefly medical unless deep abscesses are present. Such abscesses, when present, are aspirated or drained. If the disease is of moderate duration (six to seven days), there is a great probability that surgical care will play the major role, with penicillin being an essential aid but not effective as a sole agent.

5. Our patients are not treated by plaster immobilization, for it is felt that ordinary rest in bed is adequate splinting in all cases in which only medical care is necessary. Those in which deep abscesses are present or in which extensive bone involvement are noted because of delay in diagnosis, or because of a particularly massive and virulent infection, are splinted under the direction of the orthopedic consultant.

6. Weight-bearing is not permitted until x-ray studies show regression of bone lesions. Roentgen examinations are recommended every one to two weeks until the bone changes are showing regression, and then every four to eight weeks until complete healing. After complete healing, the patient should be followed every six months to a year for several years by x-ray studies.

SUMMARY

1. A report of seven consecutive cases of acute hematogenous osteomyelitis is given.

2. The importance of having a high degree of suspicion for the presence of this disease, and the early initiation of adequate treatment on only a clinical diagnosis are stressed.

3. A suggested outline for the medical treatment of acute osteomyelitis is given.

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DWARFISM OF UNDETERMINED ETIOLOGY

A Study of Birth Weight and Subsequent Development

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THIS study was carried out on a series of dwarfed children selected from the case records of the Children's Hospital in Boston. Various indices of growth and development were calculated and compared with each other as well as with the birth weights.

Case Selection.—Since the term infantilism is commonly used synonymously with dwarfism,[1] all the cases indexed under both classifications at the Children's Hospital in Boston were consulted. As indicated in Table I, certain cases were excluded from the series. For example, not only a definite diagnosis of hypothyroidism but also suggestive clinical evidence was sufficient to omit the patient from the study. There remained forty proportionate dwarfs in whom no cause for dwarfism was implicated. With similar criteria, the diagnosis of pituitary dwarfism is often made.[2] The cases selected were seen at the Children's Hospital from 1919 to the present and included both ward and clinic patients.

Table I. Selection of Cases

Total number of cases indexed as dwarfism			56
Cases used		31	
Cases not used		25	
Hypothyroidism	9		
Insufficient data	7		
Malnutrition	3		
Renal disease	1		
Rickets	1		
Achondroplasia	1		
Celiac disease	1		
Severe scoliosis	1		
Record unobtainable	1		
Total number of cases indexed as infantilism			28
Cases used		9	
Cases not used		19	
Insufficient data	6		
Renal rickets	4		
Records unobtainable	3		
Malnutrition	2		
Tuberculosis	1		
Disproportion	1		
Above normal stature	1		
Incorrectly indexed	1		

Data Used.—The cases used were those in which both height and weight measurements were recorded; in many there were multiple sets of observations

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but the study of individual growth curves was not done. In all the calculations performed in this paper only the first applicable set of observations was used, thus avoiding the weighting of the results by having more than one observation for each case in any particular correlation. A summary of the information used is given in Table II.

TABLE II. SUMMARY OF CASES

CASE	SEX	BIRTH WEIGHT (LB.)	CHRONOLOGIC AGE (YR.)	HEIGHT (IN.)	WEIGHT (LB.)	BONE AGE* (YR.)
1	M	7.50	10.2	43.4	38.0	–
2	M	6.10	5.2	37.5	28.5	4.5
3	F	5.00	7.0	38.0	30.0	3.0
4	F	7.40	5.1	39.0	28.0	4.3
5	M	–	5.4	37.8	27.8	–
6	F	6.80	5.8	39.0	34.0	–
7	F	5.00	1.6	27.0	15.0	–
			6.3	41.8	33.3	5.0
8	F	6.50	4.6	34.5	26.3	–
			5.6	37.5	31.0	3.7
9	M	–	7.8	37.9	30.3	–
10	M	8.12	4.6	38.0	33.3	–
11	F	7.00	6.8	35.0	28.0	2.0
12	F	5.75	3.8	36.0	21.9	–
13	F	5.50	4.1	36.8	24.5	–
14	M	7.00	4.8	35.5	27.8	3.0
15	F	7.00	6.1	40.8	30.3	5.8
16	M	3.00	4.4	37.0	24.8	2.0
17	M	9.50	7.4	41.0	38.3	–
18	F	1.50	1.7	25.5	11.5	–
19	F	4.20	7.0	38.0	23.3	4.0
20	M	7.60	0.9	27.0	18.5	–
			5.1	35.8	27.0	2.0
21	F	7.44	4.5	31.5	23.5	0.2
22	F	13.00?	3.2	30.3	17.1	–
23	F	5.00	1.6	31.5	19.5	–
			1.8	32.4	19.4	1.0
24	M	9.00	8.8	41.5	30.0	3.5
25	F	8.00	9.2	43.8	46.8	9.0
26	F	6.25	5.8	36.0	24.3	2.5
27	F	4.50	3.2	30.5	16.0	2.0
28	F	6.00	4.3	37.8	28.5	3.8
29	F	–	2.1	32.8	21.0	–
30	F	7.00	0.8	26.0	13.4	–
31	M	–	6.7	42.0	37.5	4.3
32	M	4.90	2.3	33.5	22.0	1.3
33	F	7.50	7.8	40.5	30.0	3.6
34	M	7.00	9.5	45.0	57.3	–
35	M	–	9.0	41.5	41.5	7.3
36	M	5.75	2.4	30.3	21.3	–
37	M	10.25	10.8	48.8	54.5	8.0
38	M	–	9.0	43.0	43.0	–
			12.8	48.5	51.5	8.8
39	M	8.25	6.9	37.0	29.0	5.0
40	F	6.00	6.9	39.5	31.8	3.3

*When given as a range, the midpoint was taken.

There were not sufficient data to allow study of birth length, race, family background, mental age, dental development, glucose tolerance tests or 17-ketosteroid excretion. Similarly, therapy was instituted in only a small number of cases and then chiefly for diagnostic purposes and with no significant height changes.

Over three-fourths of the children were brought in with a chief complaint related to retarded development.

Standards of Dwarfism.—To compare the heights of the children in this series with various standards for dwarfism, Fig. 1 was constructed. This shows a normal mean height curve[4] and the several lower limits of normal calculated therefrom. The heights observed in the dwarf series are indicated also. It is apparent that the standard for dwarfism of 70 per cent of the mean height of coevals[6] is extreme in relation to the cases studied. The upper limit of these cases corresponds most closely to the standard of height at 80 per cent of chronologic age,[5] i.e., a child would be considered a dwarf if his height were less than the normal height at 80 per cent of his age. The wide variation of these standards is worthy of note.

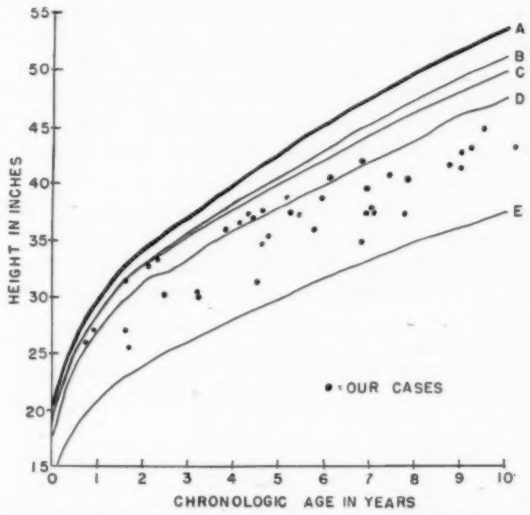

Fig. 1.—Comparison of several standards of dwarfism with cases studied.*

A, Normal mean height
B, 10 percentile
C, Normal mean height at 80 per cent of chronologic age
D, Mean height – 3 S. D.
E, 70 per cent of mean height

The normal mean height†, *A*, the 10 percentile, *B*, and the standard deviation used to calculate standard *D*[3], are from Vickers and Stuart's values for normal children[4]. Standard *C*[5] and standard *E*[6] were both derived from the values of *A*.

*These standards were calculated for boys; up to 10 years of age the growth curves for boys and girls almost coincide.

†For ages under 2 years, the height values are for measurements taken with the patient in the recumbent position.

Sex Distribution.—There were eighteen males and twenty-two females—not a significant difference—which were not considered separately in any subsequent calculations or figures.

Skull X-ray Findings.—Twenty-two of the cases had one or more skull x-rays taken. All cases so examined had negative findings.* Thus no positive x-ray evidence of pituitary pathology was observed in the group.

*One case showed questionable sellar enlargement, but was considered negative on a subsequent x-ray examination 1.3 years later.

Comparison of Mean Dwarf Birth Weight With Normal Birth Weight.—The birth weights of those in the series were compared with those of normal children. To obtain standards more comparable to the data at hand, it was decided to calculate a normal birth weight. This was done in the following manner. The mean birth year of the dwarf series was 1931; consequently the records of the Boston Lying-in Hospital for that year were consulted. A total of 117 birth weights were selected from consecutive cases about equally distributed in January, April, July, and October. This was done to compensate for normal seasonal variations in birth weights.[7] The dwarf series showed no significant monthly variation in frequency. Newborn infants not surviving their stay in the Lying-in Hospital were excluded from the normal series, as all the dwarf cases had obviously survived at least this length of time. Premature babies were not excluded provided they had filled the foregoing requirements. The Boston Lying-in Hospital records utilized were for non-private cases which strengthens their socioeconomic similarity to the group of dwarfs. The findings relative to the dwarf and normal birth weights are summarized in Table III.* There is no apparent reason why the group for which the birth weights were available (34 of the 40) should have any higher or lower mean birth weight than the dwarf group as a whole.

The difference between the birth weights of the normal children and the dwarfs is highly significant. Using other normal birth weights as standards[4, 8] gave a similar degree of significance. This makes the group of dwarfs unlike the usual concept of pituitary dwarfs who are generally stated to have normal birth weights.[3, 9]

TABLE III. BIRTH WEIGHT

	DWARF SERIES	NORMAL SERIES
Mean (lb.)	6.46	7.54
Standard deviation (lb.)	1.76	1.10
Number of cases	33	117
Critical ratio	3.3	
Probability	0.1 per cent	

Calculation of Growth Indices.—Using the height and weight standards given by Jackson and Kelly,[10]† the height and weight ages were calculated for the dwarf group. The height age of an individual is the age for which his height is normal. The weight age was derived in a similar manner. The bone ages were taken from the clinical records and had been estimated from hand and wrist bone x-rays. The developmental ages were derived from the Wetzel Grid.[11]

An index of height development was formed by means of the following formula, height age/chronologic age × 100. A weight index was similarly calculated, weight age/chronologic age × 100, as were a skeletal index, bone

*One birth weight value was omitted from the dwarf series. This was for a child claimed to be 13 pounds at birth but who only weighed 17.1 pounds at 3.2 years of age (Case 22). This birth weight value was marked with a question in the clinical record.

†It will be noted that the normals used here are different than those used in Fig. 1. Vickers and Stuart's data[4] only covered children through 10 years of age while Jackson and Kelly's standards[10] did not include values for both Standard Deviation and 10 percentile.

age/chronologic age × 100, and a developmental index, developmental age/chronologic age × 100. These four indices are measures of retardation; the values lying farthest below the normal of 100 are most retarded. Further as a measure of relative thinness, an index consisting of weight age/height age × 100 was calculated.[5]

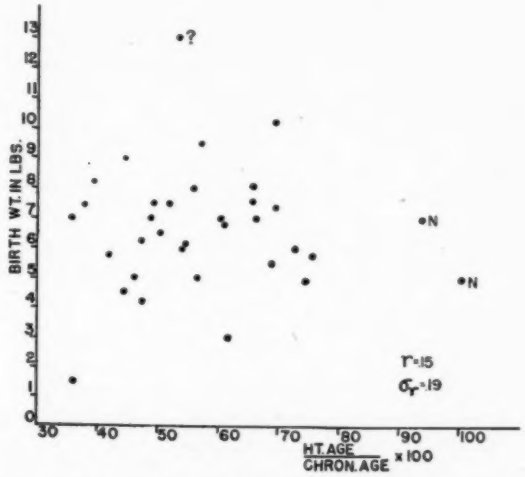

Fig. 2.—The value of r given was calculated leaving out the values of the point marked "?" (Case 22, previously mentioned in the text) and the two points marked with "N" (Cases 23 and 30, whose height age/chronologic age × 100 was greater than 80). Their inclusion would not have increased the value of the correlation coefficient, r.

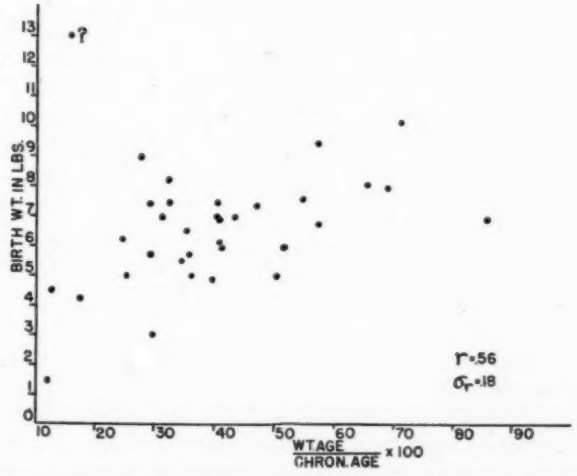

Fig. 3.—The point marked with "?" (Case 22) was not used in calculating the correlation coefficient, r.

Correlation of Growth Indices.—The results of the correlation coefficients which were calculated are shown on the respective figures. The correlations utilized the indices described above. By having ages in both numerator and denominator it was hoped to avoid certain fallacies involved in correlating two variables each of which is dependent on time.

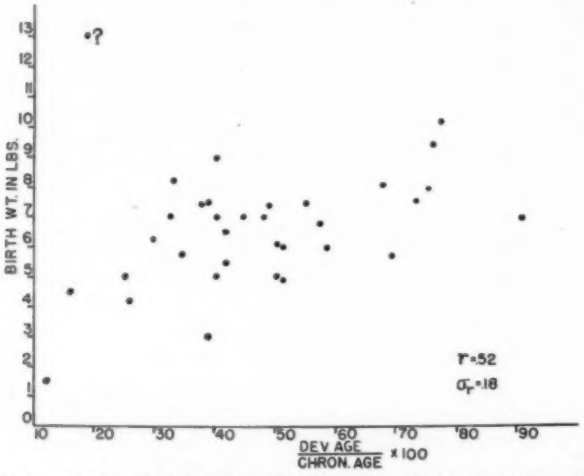

Fig. 4.—The point marked with "?" (Case 22) was not used in calculating the correlation coefficient, r.

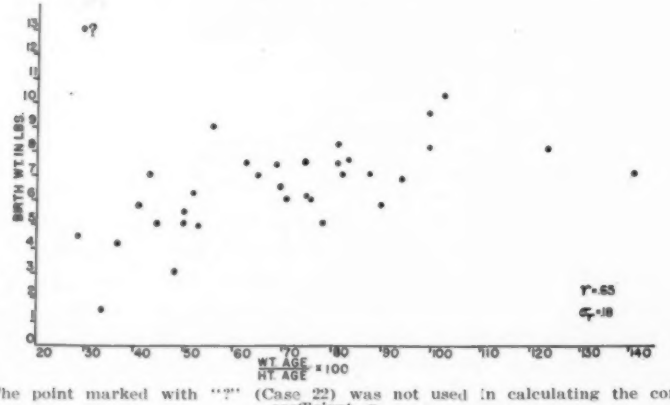

Fig. 5.—The point marked with "?" (Case 22) was not used in calculating the correlation coefficient, r.

No significant relationship was found between birth weight and subsequent height retardation (Fig. 2).

The weight retardation (Fig. 3) and developmental retardation (Fig. 4) were each directly related to the smallness of the birth weight by about the same extent. This might be expected, in view of the fact that the developmental age is so largely dependent on weight.

The correlation of birth weight with future thinness (Fig. 5) was slightly greater.

The children selected as dwarfs were of short stature (Fig. 1). As mentioned above, it was found that the dwarf group had a mean birth weight

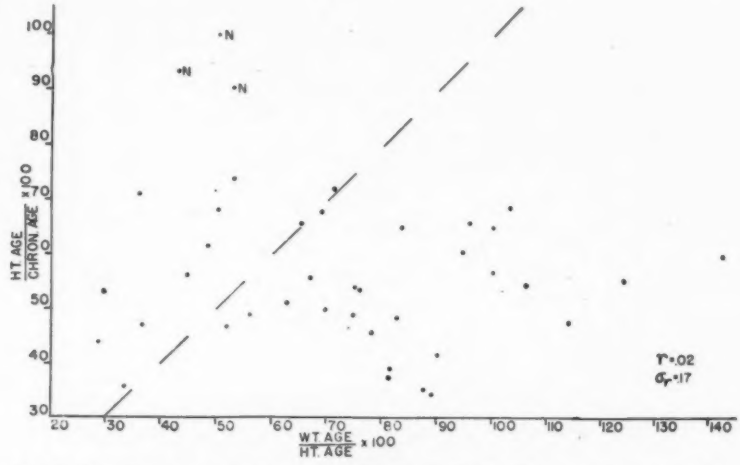

Fig. 6.—The three cases marked with "N" (Cases 23, 29, 30) were not used in the computation of the correlation coefficient, r. Their inclusion would not have increased the value of r. The broken diagonal line represents the points at which the coordinates have equal values.

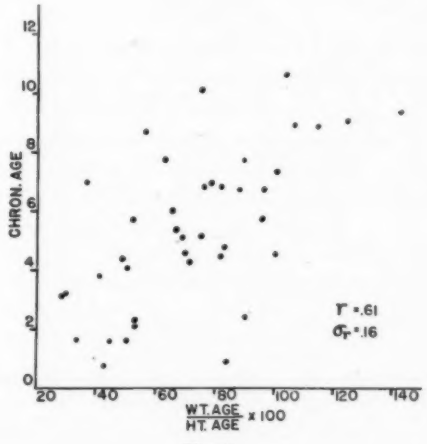

Fig. 7.

below normal (Table III). On the basis of these two findings one might have expected the shorter dwarfs to have been smaller at birth, but such was not the case (Fig. 2). An explanation of the findings may lie in the fact that as a group the dwarfs were thin and this thinness was related to the smallness

at birth (Fig. 5). The same family background leading to a poor diet in pregnancy and hence a low birth weight[12] may also have prevailed during the dwarfs' home life and so resulted in thinness.

It was found that the extent of height retardation and thinness were unrelated in the dwarf group (Fig. 6). If malnutrition had played a very large role in causing the diminished stature, and if the thinness index is a measure of malnutrition, one might have expected some correlation in Fig. 6.

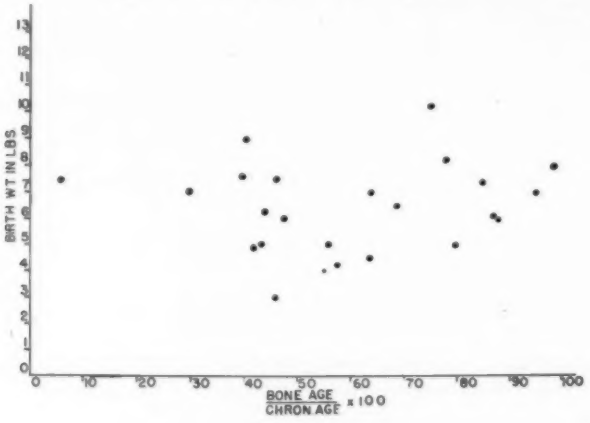

Fig. 8.

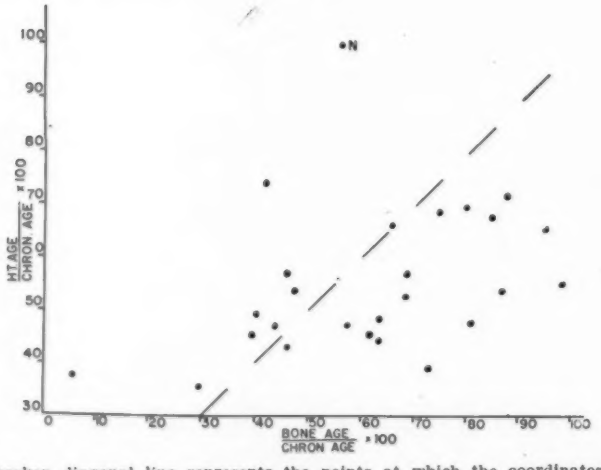

Fig. 9—The broken diagonal line represents the points at which the coordinates have equal values.

It was shown that there was a distinct tendency for the younger dwarfs to be thinner (Fig. 7). Aside from explaining this by some intrinsic developmental pattern, one should consider the possibility that in younger children mothers are more likely to note and become concerned over weight retardation than

height retardation. No striking associations were found between bone age retardation and birth weight (Fig. 8), height retardation (Fig. 9), or developmental retardation (Fig. 10). It was noted, however, that the developmental age retardation in general exceeded the bone age retardation. A difference in normals used for the Wetzel Grid and for the bone age standards could cause this picture.

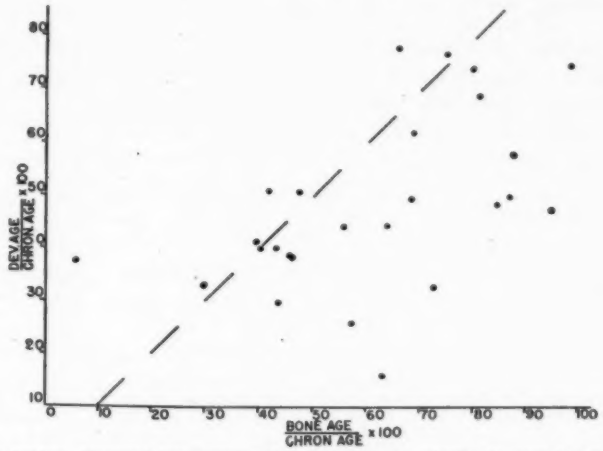

Fig. 10.—The broken diagonal line represents the points at which the coordinates have equal values.

SUMMARY

A series of forty proportionate dwarfs from the files of the Children's Hospital in Boston in whom no cause for diminished stature had been found was studied. The following conclusions were reached.

1. The most satisfactory standard of dwarfism for the series appears to be height age/chronologic age × 100 equal to 80 or less.
2. The mean birth weight of the series of dwarfs was 1.1 pounds below that of a series of comparable normal children.
3. The degree of height retardation was not related to the birth weight.
4. The weight and developmental retardation were correlated positively to birth weight.
5. There was a positive correlation between birth weight and subsequent thinness.
6. There was, however, no correlation between thinness and height retardation.
7. The degree of thinness was correlated positively to the age when first seen.

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TENSION TYPE OF CONGENITAL PULMONARY CYST

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THE large single tension type of congenital pulmonary cyst is quite rare. It usually occurs in infants and until the last decade almost always resulted in a fatality. However, with the realization that this lesion can be successfully handled surgically, these cysts have become of exceptional interest to the pediatrician, roentgenologist, and the surgeon. We are reporting the successful removal of such a cyst in a 4-month-old infant.

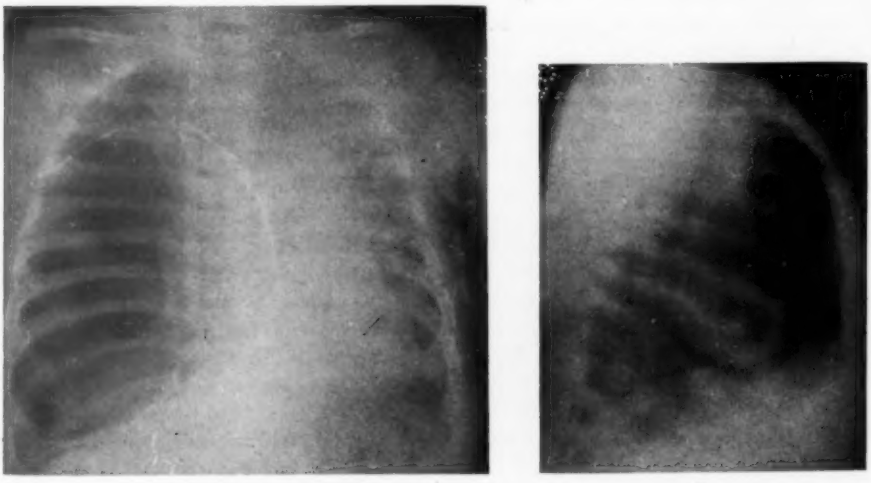
No attempt has been made to review the entire literature but in this country interest in this disease was stimulated by Koontz[1] in 1925. He reviewed the literature and reported on 108 cases of congenital cysts of the lung. In seven of these cases there were large single cysts present while in the remainder the cysts were small and usually multiple. Koontz at the time of his report felt that the case he was reporting was the first of its type in the American literature; however, he found out at a later date that Pappenheimer had reported such a case in 1912. In 1933 Anspach and Wolman[2] wrote an excellent paper on this disease. They found on a review of the literature 150 cases of congenital lung cysts and they state "only a few of these were in infants and in fewer still was the condition diagnosed and its course watched during life. In most instances the lesion was an accidental finding at necropsy." In 1936 Oughterson and Taffel[3] published a review of the subject and a case report in which an 8-year-old boy, with five independent cysts was treated surgically by converting the five cysts into a single cyst. This cyst was then treated by continuous negative pressure through a catheter until it sealed off. The boy had remained well with no evidence of recurrence for two years following surgery. In 1943 Fischer, Tropea, and Bailey[4] reported the first successful pulmonary resection, lobectomy upper and middle lobes, for congenital cystic disease in an infant. In 1946 Gross[5] published a case in which he had done a successful pneumonectomy on a one-month-old infant with the same diagnosis. In his article Gross discussed the therapeutic approach to this problem and listed four methods of value for relief of respiratory embarrassment.

1. Introduction of needle into cyst as a temporary lifesaving procedure.
2. Introduction of trocar followed by catheter into cyst for prolonged aspiration. This may be useful in collapsing cyst in preparation for surgery.
3. Marsupialization of the cyst onto the chest wall with methods of destruction of the lining membrane. This method may be used in the single cyst.
4. Enucleation of the cyst or removal of pulmonary tissue containing it. This he regarded as the treatment of choice.

Burnett and Caswell[6] in 1948 reported a successful lobectomy for pulmonary cysts in a 15-day-old infant who had been explored through the abdomen one day previously, with the mistaken diagnosis of a congenital diaphragmatic hernia. In this case a needle was introduced into the cyst without relief of symptoms following the abdominal exploration.

CASE REPORT

The family history is of interest. The mother and father are Rh positive. Their serology is negative. There have been five pregnancies. The first resulted in a miscarriage at four months. The second miscarried at four and one-half months. The third was a full-term stillborn infant. The fourth was a full-term infant who died twelve hours after delivery. Unfortunately, no post-mortem examinations were carried out.



A. *B.*

Fig. 1.—*A*, Retouched posteroanterior film to show initial size of cyst. *B*, Lateral film showing anterior position of cyst.

W. B. was a full-term white male infant born Aug. 17, 1947, weighing 7 pounds, 10½ ounces. Following delivery there was no difficulty although the mother states the child always seemed to breathe rapidly. However, on Dec. 14, 1947, there was a marked change and respirations became rapid and labored. On Dec. 16, 1947, he was admitted to the Miami Valley Hospital with rapid, gasping respirations and his color had changed to a grayish blue. Physical examination revealed a well-developed male infant weighing 12 pounds, 6 ounces, in acute respiratory distress. Rectal temperature on admission was 101.2° F. and four hours later 101.4° F. Respirations were gasping and rapid, approximately 60 per minute. The pulse rate was 160 per minute. The right thorax appeared larger than the left. The percussion note was hyperresonant over the right thorax and breath sounds were absent. There was slight dullness at the left apex with normal breath sounds over the left thorax, except at the left base where numerous inspiratory râles were heard. The heart sounds were distant and rapid and could best be heard just to the left of the left nipple. The remainder of the examination was essentially normal except for moderate abdominal distention.

Roentgenologic study showed a large, air-containing sac filling the major portion of the right thorax (Fig. 1). Atelectatic compressed lung was present at the right apex and at the right base. There was dense clouding at the left apex which appeared to be contiguous

with the mediastinum. A lateral film showed the air sac to lie principally in the anterior position. The diagnosis of a cyst of the lung was made by Dr. George Nicoll, the roentgenologist.

Course in Hospital.—A 20-gauge needle using Novocain anesthesia was immediately introduced into the cyst through the fifth interspace just lateral to the right nipple. There was

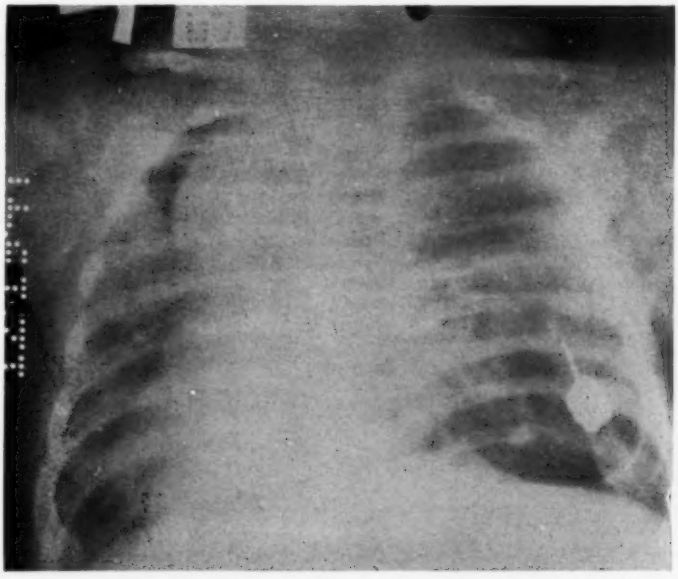


Fig. 2.—Collapse of cyst after introduction of needle.

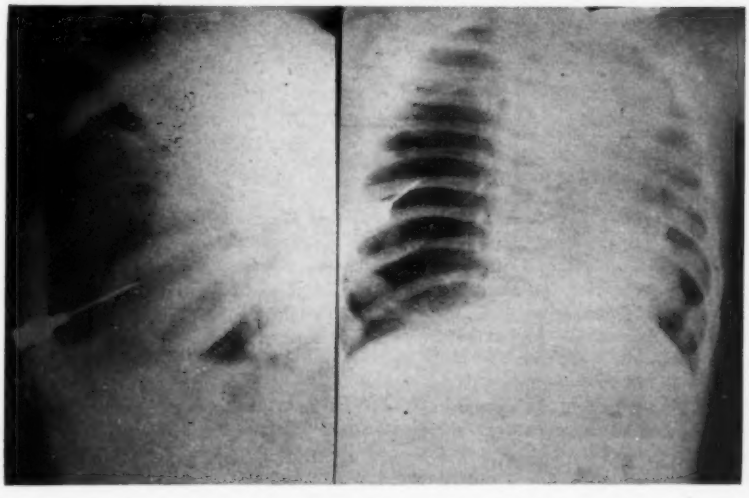


Fig. 3.—Re-expansion of cyst with needle in situ is shown in both posteroanterior and lateral films.

an immediate gush of air from the needle, and the needle was fixed in place with adhesive straps and connected to a tube. The distal end of the tube was placed underwater in a bottle. There was immediate improvement and respirations became less rapid and labored and the cyanosis disappeared. There was a steady bubbling of air into the water bottle with each respiration. The child was started on penicillin 20,000 units every 3 hours. The following day due to the fact that a moderate amount of air had leaked into the subcutaneous tissue, it was decided to introduce a catheter into the cyst. Under Novocain anesthesia a trocar was introduced through the same interspace and a catheter was placed to a depth of approximately 4 to 5 cm. Following this there was a constant flow of air through the catheter into the water bottle. However, checkup x-ray films the next day showed the catheter to be lying along the wall of the cyst and not in it. Later that day air stopped coming through the catheter and the child became dyspneic and cyanotic. The catheter was removed, and a needle was reinserted into the cyst. On two occasions during the next five days, it was necessary to change the position of the needle due to the fact that the flow of air stopped. This immediately caused the development of both dyspnea and cyanosis in the infant. By the fifth hospital day the child's temperature which had been peaking to 101° F. daily returned to normal and his general condition was improving steadily. His appetite increased and the abdominal distention which had been present had disappeared. On the tenth hospital day surgery was carried out.

Fig. 4.—Posteroanterior film four months after surgery showing shift of mediastinum back toward midline.

Operative Procedure.—The anesthesia was positive pressure endotracheal using both cyclopropane and ether; it was administered by Dr. John Valin. A cannula was inserted into the left saphenous vein just above the ankle and sutured in place. The infant was given 200 c.c. of blood during the operation.

The right thorax was prepared and draped and a right anterior incision from approximately one inch lateral to the sternum to the midaxillary line was made. The anterior portion of the sixth rib was resected subperiosteally. The thickness of the periosteum was striking. On opening the pleura the cyst bulged through the operative wound so that it was hardly necessary to use any retraction. The cyst occupied the entire right middle lobe and was intimately attached to both upper and lower lobes which were markedly compressed and

atelectatic. The cyst was opened and its wall was moderately thick. There were two bronchioles lying on the inner surface from which a steady stream of air escaped. One was situated just below the attachment to the upper lobe and one on the anterior wall approximately 1.5 cm. above the lower lobe. The cyst extended over to the left of the sternum. It was dissected free from the upper and lower lobes by the clamp-and-cut method. No true fissures were present between the cyst and the upper and lower lobes. Dissection was carried down to the hilum. A fairly good sized artery and vein leading to the cyst were present. These were from a division of the pulmonary vessels to the left lower lobe and were ligated and divided just above the point where they branched. No separate and distinct middle lobe bronchus could be identified. The cyst wall was intimately adherent to the upper lobe vessels which were displaced to the left beneath the sternum and it was decided to leave a small portion of the cyst in situ at this point. Interrupted silk sutures were used throughout except where the upper and lower lobes had been divided from the cyst. Here a running atraumatic 0000 chromic catgut suture was used. A small Pezzar catheter was placed into the right pleural cavity through a stab wound in the midaxillary line. Both the upper and lower lobes expanded well under positive pressure anesthesia and the wound was closed using interrupted silk sutures for the pleura, the periosteum, the muscle layer, and the skin. After closure all remaining air in the thorax was aspirated through the catheter, and the catheter was connected to a rubber drainage tube whose distal end was underwater.

Fig. 5.—Photograph of child two months after surgery.

Postoperative Course.—Following this operation the child was given 100 c.c. of blood during the afternoon. He was started on water, 2 ounces, eight hours after surgery, and the following morning was started on a restricted formula, 3 ounces every four hours. This was gradually increased. For the first forty-eight hours there was quite marked abdominal distention, but he had a stool following a tap water enema on the first postoperative day. Thereafter distention subsided and he had daily stools. He was kept in an oxygen tent until the third postoperative day. His temperature spiked to a maximum of 103.4° F. by rectum on the second day and then gradually declined reaching a normal level on the sixth day and remaining normal thereafter. The leucocyte count reached a peak of 25,600 with 65 segmented and 21 immature cells on the second day and declined steadily until the seventh day when the white blood cell count was 11,150 with 38 segmented and 19 immature cells. An x-ray of the chest on the third day showed the right upper and lower lobes to be expanding well with no appreciable amount of fluid in the thorax. The catheter drained serosanguineous fluid, between 100 and 200 c.c., for the first twenty-four hours and by the third day the to-and-fro movement of water in the tube had stopped, indicating the catheter had become sealed off. It was removed the following day. He was given penicillin 20,000 units every 3 hours intramuscularly and sulfadiazine orally 2½ grains every four hours through

the seventh postoperative day. A chest film on the tenth day showed the upper and lower lobes of the right lung to be completely expanded with some shift of the mediastinum and heart back toward the midline. He was discharged home on the twelfth day.

Pathologic Report.—(Melvin Oosting, M.D.) The specimen consists of an irregular piece of tissue measuring 10 cm. in length and ½ mm. in thickness. It is fibrous in character with small pieces of lung tissue attached.

Microscopic examination shows the wall to be lined with a respiratory type of epithelium on a base of fibrous connective tissue and smooth muscle. There are occasional islands of cartilage present and a number of well-defined bronchioles and bronchi. One side of the wall is covered by pleura showing areas of relatively recent nonpyogenic inflammatory reaction. On another part of the wall islands of collapsed and aerated alveoli may be seen. Some of these contain recent hemorrhage with large phagocytes containing blood pigment. This has the appearance of a congenital cyst of the lung.

Subsequent Course.—This infant has had an uneventful follow-up with no respiratory difficulty for six months following surgery. Roentgenograms at two and four months showed complete expansion of the right upper and lower lobes with farther shift of the mediastinum toward the midline.

DISCUSSION

The so-called congenital tension cyst of the lung is simply a bronchiogenic cyst arising in pulmonary tissue. These cysts arise due to an abnormality in the development of the bronchial tree. They may arise within lung tissue or adjacent to it if the continuity of the bronchial tree is maintained. However, it is quite common for a mass of cells to be completely pinched off during embryologic development and in this case a cyst may be completely separate from the bronchial structures. This is a fairly frequent occurrence and explains the development of bronchiogenic cysts in the mediastinum. These congenital cysts all have a common histologic appearance. They are lined by ciliated columnar epithelium with smooth muscle and elastic tissue in the wall. Cartilage is frequently present as well as mucous secreting glands. In contrast, the inflammatory cyst has simply a fibrous tissue lining, but often there may be a superimposed inner layer consisting of inflammatory cells and macrophages. If marked infection has occurred within a congenital cyst causing destruction of the lining membrane and of the cyst wall, then the diagnosis of whether a cyst is of congenital or of inflammatory origin is difficult.

Congenital cysts are usually quite small, containing mucoid secretion. They may cause no symptoms and remain quiescent. However, occasionally one may encounter a tension cyst which develops rapidly and causes marked respiratory embarrassment. The cause for the sudden enlargement is obscure. It is best explained by a ball valve type of mechanism in which air can enter the cyst but cannot escape as rapidly as it enters. This may be due to a twisting of a bronchus or bronchiole or to edema which partially occludes the lumen so that the egress of air is impeded. In this case at operation there were two definite small bronchi present. Their course was long and tortuous and it was easy to see how the outflow of air might be partially or totally blocked. The reason why this type of cyst is found primarily in infants is due in all probability to the elasticity and pliability of the pulmonary tissue which allows for rapid expansion of the cyst within the lung and concurrently the cyst as it increases in size is allowed by the mobility of the mediastinum to push over into the opposite thorax.

The differential diagnosis must include congenital diaphragmatic hernia, emphysematous blebs of the lung, and tension pneumothorax. The first is ruled out by the administration of barium by mouth. The air-filled loops of bowel in the thoracic cavity will fill with the opaque medium and the diagnosis will be made. Anspach and Wolman[2] in 1933 pointed out how a congenital diaphragmatic hernia might simulate congenital cysts, and they recommended the use of oral barium to avoid such a mistake at that time. Emphysematous blebs of the lung at times may be difficult to differentiate, but usually they are thin walled and on the pleural surface, and the diagnosis can be readily made. Tension pneumothorax can be diagnosed quite easily by the roentgenogram. Once the diagnosis of a tension cyst has been made, with signs and symptoms of respiratory embarrassment present, immediate therapy aimed to relieve the tension in the cyst is in order. This may be done in one of several ways, either by decompression with a needle or catheter or by immediate surgical intervention. It is our feeling that with the large tension type of cyst, needle or catheter decompression should be the first step. This may well be a lifesaving procedure. There are certain dangers in both needle and tube decompression of such a cyst. It is possible for air to leak into the pleural cavity, thus causing a tension pneumothorax. This might be fatal and the infant must be watched closely for this. In our case a subcutaneous emphysema developed due to air leaking into the subcutaneous tissue about the needle. This was not serious and was relieved by a change of position of the needle to stop the leak. On one occasion a trocar followed by a catheter was introduced into what we thought was the cyst. There was a constant bubbling of air into the water bottle to which the catheter was attached, but an x-ray the following day showed the catheter to be lying along the wall of the cyst between it and the parietal pleura. The air was leaking out of the cyst through the trocar hole and the catheter was not in the cyst proper. On two occasions while the cyst was being decompressed there was a recurrence of dyspnea and cyanosis. Each time we were warned that this was going to develop, as the continuous flow of air into the water bottle had stopped. The cause for this was an obvious block at the end of the needle. The marked increase in pressure within the cyst, when this occurred, was well illustrated by the fact that when we changed the position of the needle, the plunger of a 10 c.c. syringe which was attached to it was blown out of the barrel onto the floor. These complications are not serious if attended to promptly, but we mention them to show the associated dangers of decompression and to stress that these infants need close supervision. It is undoubtedly safer to decompress with a small mushroom type of catheter which has been well fixed, than a needle, if the catheter has been placed in proper position initially. With proper decompression it is possible to relieve both respiratory and circulatory embarrassment and to return the physiology of the chest to a more normal state. At the same time a pneumonitis which may be associated with a compression atelectasis can be treated by chemotherapy and if need be the infant can receive blood, electrolytes, proteins, etc., so that the patient becomes a good surgical risk rather than a poor one. After this has been accomplished, we feel removal of the cyst is indicated. Infants and children tolerate pulmonary surgery well. Partial

pulmonary resection, lobectomy, or even pneumonectomy are much easier procedures in an infant than in an adult. The vascular and bronchial trees may be dissected out with ease and the structures readily identified. The hilar structures are thin and pliable and there is not the fixation and fibrosis that one usually finds in the adult due to an old inflammatory process. We wish to stress that the surgeon should not have a rigid plan of operative procedure before opening the chest, but this should be flexible as the operative findings may change the entire procedure. For example in our case we were not sure whether or not a pneumonectomy would be necessary (see Fig. 1). Instead, it was possible to enucleate the cyst almost completely except for a small portion which was left overlying the vessels to the upper lobe. It might be said that since the cyst occupied the entire right middle lobe, we actually carried out a lobectomy. The point is equivocal since very little if any normal pulmonary tissue was removed. The upper and lower lobes which were markedly atelectatic expanded well under positive pressure anesthesia after the removal of the cyst and on the third postoperative day, x-ray examination showed them to be almost completely expanded. It is our feeling that to conserve normal pulmonary tissue is always worth while when the success of the surgical procedure is not jeopardized by so doing. We fully realize that at times it may be necessary to sacrifice an entire lung, but this should be determined only after careful operative examination. This infant has now been followed for six months. Roentgenograms of the chest taken two months after surgery showed complete expansion of the right upper and lower lobes, with a shift of the heart and mediastinal structures back toward the midline. An x-ray at four months showed even farther shift toward the midline. The mediastinal structures are still displaced slightly to the left, but we feel that in a short time they will be back in their normal position. The child has been completely free from any respiratory difficulty since surgery.

CONCLUSION

1. Congenital tension cysts of the lung in infants are amenable to surgery.

2. Decompression of the cyst by needle or catheter may be a lifesaving procedure.

3. With decompression of the cyst and supportive therapy the surgical risk may be changed from bad to good.

4. Removal of the cyst either by enucleation or by excision of pulmonary tissue containing it is the treatment of choice.

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ACNE NEONATORUM

Report of Acne Vulgaris in Two Infants

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INFANTILE acne is of interest not only to pediatricians but also to dermatologists and endocrinologists because the presence of its lesions raises the question, not as yet satisfactorily answered, of its causation: whether the active role is to be attributed to hormones or to some extraneous factor or factors. As against the acceptors of the theory of hormonal causation, its opponents assume that the sebaceous glands are more or less dormant in infantile life, that they do not become active until puberty, and, therefore, that they are incapable of a causative role in any difficulty of an earlier age. On the other hand, followers of the "hormone school" believe that hormonal influence exists soon after birth and so may be a cause of acne among infants, although it should be explained that its effects are to be understood as derived from the mother and as the result of her pregnancy. Wiener[1] in his excellent text remarks: "The comedones and false milia, i.e., the false enlarged sebaceous glands and the sometimes observed acne of the newborn (also his vigorous lanugo growth) have often been interpreted as hormonal pregnancy reaction." He further states: "One has even, in view of the numerous gonadal stimulations, spoken of a 'miniature puberty.'" Nor is Wiener alone in this conception of the etiology of acne vulgaris in infants, for Jacquet and Rondeau[2] too regard the sebaceous glands as active but in a secondary phase deriving from hormonal factors in the mother. As against this position, others like Kraus[3] regard the hormonal effect as "not proved" since they see the common blood circulation during pregnancy as without any special significance in this particular.

However, it is clear that acne vulgaris exists among infants. Leiner[4] remarks upon his observation of many cases of true acne, not milia: These are cases of acne punctata among infants and children ranging from 3 to 12 months in age. In accounting for this, Sulzberger and his colleagues[5] join with the majority group of writers already cited in attributing acne to the stimulation of the pilosebaceous apparatus by hormones at that time when the maternal and therefrom, probably, the fetal circulation, contain the highest index of hormones, e. g. prolans and estrins. Ordinarily, according to these same writers, this activity ceases at birth and is not resumed until puberty when the individual attains his own sex hormones. Further, their belief that the stimulation of the pilosebaceous apparatus depends directly or indirectly on the hormones, helps to explain the acne vulgaris of adolescence. Belisario[6] may be mentioned among others who believe that infant acne is somehow related to hormonal influence. The present writer himself has inclined to the hormonal theory and

it is his conviction that in the two cases of acne vulgaris of which this paper treats, hormones provide the etiologic background. For example, in connection with them there persisted for several weeks as a concomitant feature a mastitis neonatorum, a fairly common condition which is generally interpreted as indicating that gonads are at work, and which may be explained as resulting from the transfer of hormones from the mother to the infant via the placenta. It is reasonable to believe that such a transaction may at once engorge the breasts of newborn infants and stimulate the quiescent sebaceous glands, with acne resulting. As Belisario[6] writes, reporting a case of infant acne from Australia: "The general belief now appears to be that some form of inbalance of the endocrine glands, in particular as it is evidenced by exacerbation around the menstrual cycle, plays a leading part in the etiology of acne." On the other hand, various extrinsic factors have been held accountable for acne in infants, among them the indiscriminate use of oils and ointments, the use of camphorated oil, and the rubbing of the child's face with a shawl. Slavens[7] sponsors the theory that occlusion of the facial glands by oils and ointments is responsible for the formation of comedones and subsequently for acneform eruptions. Both Dore[8] and MacLeod[9] indict the local use of camphorated oil as playing a definite etiological role in the cases coming under their observation, while Harries[10] reports at least one case in which trauma, produced seemingly by the presence of a shawl, caused acne. Leiner[4] points out a more general causative relationship, observing that most of the infants he saw showed weakness and ill-health. Crocker[11] believes that the etiology of infantile acne is different from that of postpuberty, and considers warmth and moisture as combined etiological factors in infant acne. He cites for evidence the case of a 3-year-old girl who was treated for a laryngeal obstruction with repeated linseed poultices and whose back and lower chest thereafter presented scattered comedones mingled with acne papules and pustules. However, the force of this observation is somewhat reduced by his admission that a bacterial factor too may have operated. To most observers also a sex difference appears, male infants apparently being affected more often than female infants.

CASE REPORTS

CASE 1.—The mother of C. P., a white male infant who was seen when he was one week old, noticed soon after birth that his cheeks were blotchy. A week later numerous milia appeared upon the skin of the forehead and of both cheeks and were followed by blackheads. At this time too several small pustules were noticed upon the right side of the face and forehead. Until the age of 3 weeks the infant was fed exclusively upon breast milk when a simple dilution of evaporated milk and water with milk sugar was added. The mother was enjoying good health; she denied taking any medication including bromides and iodides. For cleansing only pure olive oil and castile soap and water were used upon the infant. When first he was seen, the infant exhibited engorged breasts, which subsided spontaneously after ten days; otherwise, the physical examination was negative. An ointment (3 per cent of precipitated

sulphur in zinc ointment U.S.P.) was prescribed after the use of resorcinol (1 per cent in 70 per cent alcohol) failed to bring about improvement. The lesions had entirely disappeared six weeks after the patient was first seen. Thereafter monthly checkups failed to show any return of the acne. At the age of 9 months the infant was happy and in good health upon the sort of diet indicated for that particular age. Only a small scar upon the right cheek marked the site of one of the pustules.

A. *B.*

Fig. 1.—Case 1, C. P., a male infant. Photograph taken at 10 weeks of age. *A*, Note papules and comedones upon both cheeks and forehead. *B*, Profile. Note comedones and pustules upon right cheek, also pustule above right eyebrow.

Case 2.—A female infant of Italian parentage was first seen at the age of 3 months at the Skin and Cancer Hospital in Philadelphia. The lesions consisted of papules and comedones upon the skin of the forehead, cheeks, and chin. The mother first noticed the "pimples" upon both cheeks when the infant was 4 days old; and these were followed in the same locality by blackheads a month later. There were no other lesions. The patient was a full-term, bottle-fed infant who had received no medication containing bromides or iodides, nor had iodized salt been used in the preparation of her food. As in the former case, inquiry revealed, that a few days after birth the infant's breasts had become enlarged and had remainded engorged for almost three weeks. Physical examination was negative. There was a hemoglobin of 75 per cent; red blood cells, 3,900,000 per centimeter; white blood cells, 7,900; polymorphonuclear leucocytes, 53 per cent; monocytes, 1 per cent; lymphocytes, 46 per cent. The blood sedimentation was 8 mm. in one hour (Wester-

gren). Therapy consisted of the use of soap and water followed by the local application of the official lotio alba, N.F. one-quarter strength, but this worked no improvement. Then a lotion (2 per cent resorcinol in 70 per cent alcohol, U.S.P.) was prescribed for application three times daily, again without effect. For a third prescription, 3 per cent precipitated sulphur in zinc oxide ointment, U.S.P., was ordered and an almost immediate improvement followed its use. The infant was seen again four months after her first visit to the hospital and at that time her skin was perfectly free of acne.

Fig. 2.—Case 2, M. A. S., a female infant. Photograph taken at 3 months of age. Note papules and comedones upon both cheeks, chin, and forehead.

SUMMARY

1. Two infants, one male, aged one week, the other female, aged 3 months, both presented typical lesions of acne vulgaris.

2. These cases and other cases among infants reported in the literature seem to indicate that acne vulgaris is not so uncommon among newborn infants as has hitherto been believed. Careful examination of the skin of the newborn infant would probably reveal the presence of papules, pustules, and comedones in a much greater frequency than that in which they have been assumed to occur.

3. The mastitis neonatorum concomitant with or preceding the acne vulgaris suggests the correctness of the preponderant opinion that infantile acne is dependent upon the gonads and results from stimulation of the sebaceous glands.

4. The use of a topical ointment containing 3 per cent of precipitated sulfur in a zinc oxide base resulted in a prompt improvement of the lesions.

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INCIDENCE OF DISEASES AMONG READING FAILURES AND NONFAILURES

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SOME children of normal or superior intelligence fail to learn to read, even when exposed to teaching that is adequate for the majority of children. The condition is usually called, "reading difficulty," although other terms include, "alexia, word-blindness, reading disability, and strephosymbolia." Sometimes such cases are subdivided into functional and organic groups, the latter being referred to as having "specific reading disability." This implies the presence of some lesion which results in weakness of the language function, accompanied, according to some, by lateral dominance variations.

Reading difficulty exhibits an hereditary tendency and occurs more frequently in boys than in girls. Almost no pathologic studies of the brains of reading difficulty cases have been reported. Hinshelwood[1] is credited with a single necropsy. This appears to have contributed to his conclusion that a lesion in the left supramarginal and angular gyri in a right-handed person might cause reading failure. However, much more recently Orton[2] pointed out the fact that no pathologic condition of the visual memory center had been demonstrated up to that time.

A great deal of investigation of possible causes of reading failure has been carried on, but it has not been as productive as one could wish because of the variation in the preparation for research and the background of the investigators. For example, physical studies have been made by physicians, psychologists, optometrists, teachers, and others, using all kinds of techniques ranging from the conventional to the bizarre. It is no wonder that there has been so little agreement between them. Sometimes relatively comparable data have been interpreted quite differently by investigators with different backgrounds and divergent points of view. Out of the great mass of studies one major fact has emerged. There is no single cause of reading failure. Each case presents a constellation of etiological factors, varying from person to person and including such things as physical, emotional, psychological, social, and pedagogic components.

The present study was made in order to contribute somewhat to the understanding of the part played by physical factors in reading difficulty cases. Eight hundred seventy-five reading failures were compared with 486 nonfailures as to the frequency of various groups of diseases and defects. The median age of the reading failure group was 9 years, 7 months, while that of the control group was 11 years, 7 months. The median intelligence quotient of the reading failures was 102, while the controls presented a median of 103. The records of each child were studied, the defects and diseases were tabulated, and the frequency

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of each was calculated. In the statistical material that follows, the word "diseases" includes diseases and defects except as noted.

It was found that the reading failure group exhibited 21.1 per cent more frequent disease than did the control group. This supports a similar trend noted in an earlier study.[3] When the various classes of diseases were considered separately, smaller differences were displayed, but there was a general tendency for the reading failures to exhibit the higher frequency. Speech defects and diseases of the mouth, nose, throat, and ears (exclusive of dental conditions) displayed the greatest differences, while diseases of the eyes (exclusive of eye defects), diseases of the circulatory system, and diseases of the urogenital system exhibited medium differences between the groups. Table I presents the complete tabulation by classes of disease, while Table II lists the various diseases encountered in each.

TABLE I. COMPARISON OF FREQUENCIES OF DISEASES OR DEFECTS AMONG READING FAILURE AND NONFAILURE GROUPS

DISEASE GROUP	READING FAILURE (%)	NONFAILURE (%)	DIFFERENCE (%)
Total disease	36.1	15.0	21.1
Malnutrition	0.2	0.0	0.2
Deficiency diseases	1.4	2.0	-0.6
Alimentary tract	0.3	0.2	0.1
Mouth, nose, throat, and ears	7.8	3.2	4.6
Lungs	0.4	0.0	0.4
Circulatory system	2.5	0.4	2.1
Blood and blood-forming organs	1.1	1.6	-0.5
Endocrines	2.6	1.6	1.0
Bones and joints	0.9	0.0	0.9
Urogenital system	2.6	0.4	2.2
Skin	0.1	0.0	0.1
Allergy	1.2	0.6	0.6
Nervous system	2.2	1.2	1.0
Specific infectious diseases	0.4	0.0	0.4
Speech defect	6.2	1.2	5.0
Eye diseases	4.7	2.6	2.1

A previous study[4] involving 1,000 reading failures, including the cases used in the present investigation, reported differences in the frequencies of predominantly ocular factors; visual acuity, amblyopia, refraction, muscular imbalance, fusion, lateral dominance in terms of eyedness and handedness, and the speeds of word and object perception. It showed that hypermetropia of one diopter (D.) or more, exophoria of 6 or more prism diopters at the reading distance, and retarded speed of word perception occurred over 10 per cent more frequently among the reading failures. The differences in frequencies between the reading failure and control groups were considerably higher than in the frequencies of the physical conditions reported in the present study. For example, hypermetropia of one diopter or more occurred 30 per cent more frequently among the poor readers, while exophoria of 6 or more prism diopters at the reading distance occurred 11 per cent more frequently in the same group. The reading failures also exhibited 24 per cent more frequent retardation in the speed of word perception.

TABLE II. DISEASES ENCOUNTERED IN READING FAILURE AND NONFAILURE GROUPS

DISEASE GROUP	READING FAILURES	NONFAILURES
Nutrition	Malnutrition Celiac disease	None
Deficiency diseases	Avitaminosis	Avitaminosis
Alimentary tract	Colitis Megacolon	Megacolon colon
Mouth, nose, throat and ears	Deviated septum Nasal obstruction Enlarged uvula Diseased tonsils Sinusitis Perforated eardrum Granulations in nasopharynx	Diseased tonsils Deviated septum Sinusitis
Lungs	Tuberculosis Empyema	None
Circulatory system	Cardiac disease Patent ductus arteriosus	Rheumatic heart Patent ductus arteriosus
Blood and blood-forming organs	Purpura Anemia	Anemia
Endocrine	Hyperthyroidism Hypothyroidism Diabetes Fröhlich syndrome	Hyperthyroidism Hypothyroidism Diabetes
Bones and joints	Spina bifida Osteitis deformans Clubfoot Deformities of second fingers and toes Deformities of arms Bifid terminal phalanx	None
Urogenital system	Undescended testis Absence of left testis Kidney disease Enuresis Diabetes insipidus	Enuresis
Skin	Alopecia areata	None
Allergy	Unspecified	Unspecified
Nervous system	Anesthesia of toes Birth palsy Bell's palsy Brachial palsy Epilepsy Facial tics Hydrocephalus Paralysis left leg Parkinson's syndrome Postconcussive state Rathke pouch cyst Trauma (brain)	Birth palsy Facial tics Migraine
Specific infectious diseases	Chorea Syphilis	None
Speech defects	Unspecified	Unspecified
Eye diseases	Anisocoria Cataract Choked disc Corneal scar Chalazion Chorioretinitis Deformity of left pupil Fixed left pupil Hordeolum Hole in macula Nystagmus Ptosis Neoplasm Persistent hyaloid artery Color blindness Occlusion of tear duct	Cataract Chronic conjunctivitis Coloboma Nystagmus Opaque nerve fibers Retinitis Retrobulbar neuritis

Although the results of the present comparison show a greater frequency of disease among the reading failures as compared with nonfailures, the differences in frequency in individual diseases is not great in relation to the whole group. When one considers the proportion by which the frequency is higher in the reading failure group than in the control group, it is noted that the diseases of the urogenital system and of the circulatory system are each more than six times as frequent among the reading failures, speech defects more than five times, and diseases of the mouth, nose, throat, and ears, and allergy more than twice those of the control group. Furthermore, certain conditions encountered among the reading failures were not met at all in the control group. These included malnutrition, diseases of the lungs, diseases of the bones and joints, diseases of the skin, and specific infectious diseases.

Clinically it is well known that certain diseases often interfere with learning and are important in that connection when they occur. For example the improvement in schoolwork, including reading, is usually prompt when a hypothyroid child is treated successfully. Therefore, the fact that a disease occurs more or less infrequently in large groups of reading failures should not lead one to ignore it as a possible handicap to learning.

Treatment of reading difficulty cases falls into two main divisions. First, any unfavorable physical conditions which might reduce the child's ability to compete physically or mentally with others of his own age should be corrected or treated. It then becomes the job of the teacher to instruct the child up to the limit of his ability to learn to read. In recent years education has developed many efficient techniques for remedial teaching in the field of reading. They include a large number of new approaches in addition to the old and cumbersome alphabet, phonic, and kinesthetic methods. At present there are some remedial schools, especially in the larger centers. Many private and public schools maintain a reading specialist who is trained in remedial teaching; other schools, having no one appointed for this particular job, maintain one or more teachers who have taken special work in remedial reading instruction and who are able to devote part of their time to such work. Some localities have none of these facilities and find it necessary to fall back on the summer school or camp which offers remedial teaching, the private remedial reading teacher, or individual instruction by a well-trained grade-school teacher.

SUMMARY

Diseases or defects were found to be 21.1 per cent more frequent among 875 children who were failing in reading than among 486 children who were successful in learning to read. The different classes of diseases encountered and the treatment of reading failure are discussed briefly.

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Case Reports

BONE FORMATION IN SKIN AND MUSCLE: A LOCALIZED TISSUE MALFORMATION OR HETEROTOPIA

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THE formation of mature, well-developed bone within human skin, subcutaneous tissue, and muscle is an occurrence as striking as it is rare. To the three cases reported in the literature as occurring in children, we wish to add a fourth.

CASE REPORT FROM CHILDREN'S ORTHOPEDIC HOSPITAL

A white female infant was born prematurely on April 8, 1944, weighing 3 pounds, 15 ounces. The parents were 26 and 30 years old. There was one sister aged 5 years. The family history was irrelevant. The baby was kept in an incubator for one month and did well on Olac formula. She received vitamin supplements in correct amount and variety and developed in normal sequence. Immunizations were given for diphtheria, pertussis, and variola. Illnesses included occasional respiratory infections and scarlatina without sequelae.

When the infant was removed from the incubator at the age of one month, a small, hard, irregular area was noted near the left breast. On advice of a physician, the baby was put in sunlight a few minutes each day for a week. The skin along the radial aspect of the left arm thereupon became redder than that over the rest of the body and so remained. At 5 months a reddened, apparently nontender lump was noted at the tip of the left second finger. This was believed to be a splinter and was treated with hot packs. At 6 or 7 months a small mass was noted in the left axilla. At 7 months raised areas suddenly appeared on the left forearm and on the dorsum of the left hand and continued to enlarge very slowly. At 18 months of age a particle of calcareous deposit was removed from the left second finger. This deposit subsequently recurred. At 2 years and 9 months another particle was spontaneously extruded from the distal end of the left middle finger. At 3 years, 5 months a small lump was noted in the scalp at the crown of the head.

When 3½ years old the baby was brought to the Children's Orthopedic Hospital. Routine blood studies showed normal hemoglobin, white count, and differential. The Mantoux was negative in 1 to 10,000 dilution and the Kahn was negative. Urinalyses were consistently normal. The urinary calcium excretion for twenty-four hours was 0.21 Gm. Serum calcium ranged from 8.1 to 11.8 mg. per cent. Serum inorganic phosphorus varied from 3.4 to 3.6 mg. per cent. The alkaline phosphatase was 3.8 Bodansky units.

Radiographs submitted with the patient showed apparent calcification in the soft tissues of the left axilla, arm, forearm, hand, and fingers. Recheck films in the hospital (Figs. 1, 2) were similar, but, in addition, showed an irregular destructive process at the distal end of the ulna with some periosteal reaction. Films of the right arm, skull, spine, pelvis, and legs showed no abnormalities.

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Presented before the North Pacific Pediatric Society, Spokane, Wash., March 20, 1948.

At this time two rather extensive explorations and dissections of several presumably calcified areas were done. Masses were removed from the left hand and forearm, upper arm, axillary fold, and chest wall. Some masses were intracutaneous, while others were in the subcutaneous tissue freely movable beneath the overlying skin. Some of these pieces were firmly attached to the underlying bony structure. Some were within the muscle or muscle sheath. These masses were white and varied markedly in size and thickness. (Fig. 3.) The edges were very irregular. No abnormality of the blood supply was noted. The distal joint of the middle finger was immobile with stony-hard, subcutaneous

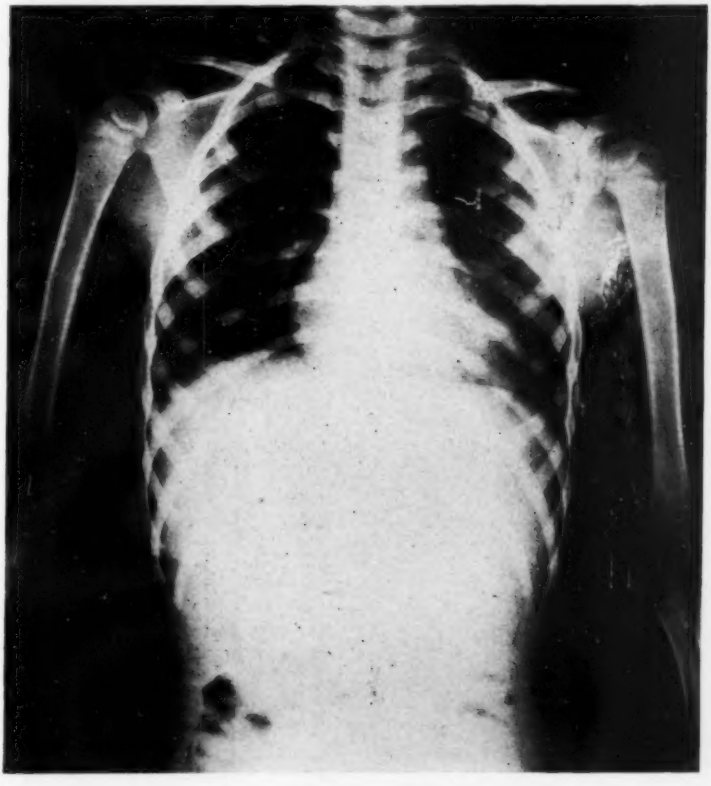

Fig. 1.—Radiograph showing heterotopic bone formation in muscle and muscle sheath, left axilla and arm.

masses firmly attached to the skin and bone at the site of previous, partial excision. The largest single piece lay on the dorsum of the left hand. It measured 1.5 by 3.5 by 0.4 cm. There was loose areolar tissue between this mass and a similar bony mass beneath it which was attached to the metacarpals. A mass in the left anterior axillary fold was attched to the undersurfce of the skin and measured 1 by 2 by 0.2 cm. This piece was quite irregular with rough edges. An associated underlying mass lay within the sheath of the pectoralis muscle at its insertion, 1.5 cm. in diameter in the widest portion, tapering toward the anterior end and splitting rather widely toward the humerus.

Following these operations, the incisions healed without incident and without recurrence of the lesions. A full-thickness graft of skin grew satisfactorily upon the dorsum of the hand. The child remained in excellent health.

Fig. 2.—Radiograph showing heterotopic bone formation in muscle subcutaneous tissue and skin, left forearm, hand, and fingers.

Microscopic examination of the surgical specimens showed not mere amorphous calcification, as was expected, but actual mature bone situated within the dermis and subcutaneous tissue (Fig. 4), within fascia and within muscle (Fig. 5). This bone possessed recognizable Haversian systems and centrally placed islands of well-formed red and fatty marrow. There were no inclusions

of cartilage and but small areas of osteoid at the periphery of the plaques where there were narrow mantles of fibrous tissue. The picture was such as to suggest at once congenital or developmental origin of the aberrant bone. There were no evidences of inflammation or of neoplasm.

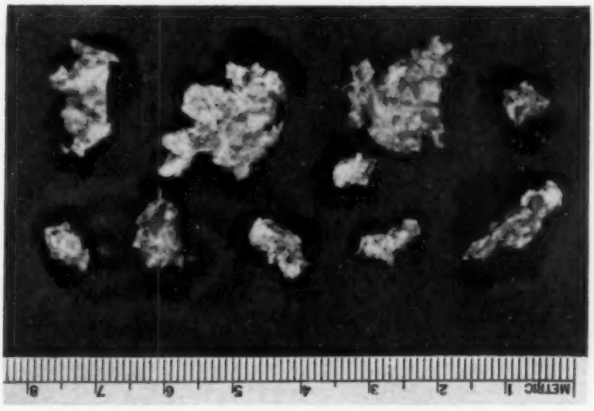

Fig. 3.—Portions of heterotopic bone removed from muscle and subcutaneous tissue, left upper extremity.

Fig. 4.—Microphotograph ×40, heterotopic bone in dermis and subcutaneous tissue from dorsum of left hand. Note fatty marrow between trabeculae of bone. (Epidermis at top of figure).

A search of the literature has yielded only three other studies dealing with children.

1. Sherwell[1] and Coleman[2] of New York City reported a 6-year-old girl with plaques in the skin and subcutaneous tissue of the left fourth toe and the sole of the left foot.

2. Taylor and MacKenna[3] of Liverpool, England, reported a 15-month-old girl with "gristly plaques" in the deeper layers of the skin distributed on the medial aspect of the right leg, on the outer side of the left thigh, on the left forearm, on the anterior and posterior aspects of the chest, and on the scalp.

3. Vero, Machacek and Bartlett[4] of New York City reported a 3-year-old boy with "lumpy" plaques in the skin of the left side of the scrotum, the left thigh, left leg, left foot, left buttock, and the back. The scrotal lesions were noted at birth, and the others developed in groups, from the age of a few weeks to 2 years. As in our case, there was spontaneous extrusion of small concrements, mainly on the toes, which first became reddened, swollen, an tender; there were also deeper seated intramuscular masses of bone developed within the left buttock and in the left popliteal region.

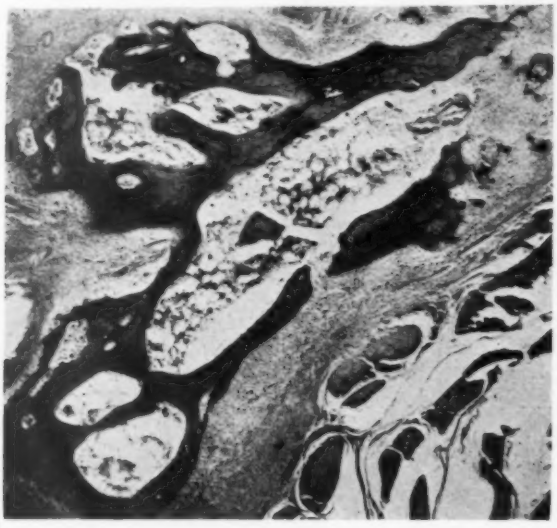

Fig. 5.—Microphotograph ×40, heterotopic bone in left pectoral muscle. Note hemopoietic marrow between trabeculae of bone. (Remnant of muscle in lower right-hand corner of figure.)

In these three cases, as in ours, biopsy of the plaques demonstrated not mere calcification, but mature bone with marrow situated within the deeper layers of the dermis. The lesions were multiple in all cases, though varying considerably in number and extent. Though the follow-ups in these cases were rather limited, there seems to be agreement that the lesions did not recur when removed. In one of the cases new lesions appeared at other sites following removal of some of the plaques. In none of the cases was there a history of antecedent trauma, inflammatory process, or other possible inciting agents. The condition was designated "osteosis of the skin" by the first authors, "osteoma cutis" by the second group of authors and "congenital osteomas of the skin" by the third group.

It is our feeling that the development of plaques of mature bone within the deeper layers of the dermis, within the subcutaneous tissue, and within muscle is a localized tissue malformation, properly designated as a heterotopia—a formation of normal tissue at an abnormal site. The segmental distribution

of the lesions, apparent both in our case and in the case of Vero, Machacek, and Bartlett,[4] is reminiscent of that occurring in some other structural developmental abnormalities such as fibrous dysplasia of bone of Albright and collaborators[5] and of Lichtenstein and Jaffe.[6]

The condition under consideration is to be differentiated from the types of calcinosis, processes in which amorphous calcium is deposited in tissue. Localized calcinosis usually occurs in adults. Disseminated calcinosis occurs more often within the first two decades of life. It is sometimes associated with scleroderma, or with Raynaud's disease or other type of vasomotor abnormality. Both the localized and disseminated forms are rare and of unknown origin.

In traumatic ossifying myositis, formation of actual bone may follow deposition of calcium in muscle that has been subject to trauma. This is a hazard of football and other vigorous occupations of adolescence.

Progressive ossifying myositis is a rare disease with familial incidence, affecting male persons predominantly, extending into adult life. Plaques of bone are formed in continuity with the skeleton, and in addition plates of bone appear within fascial planes between the muscles. In three-fourths of the reported cases, the great toes are abnormally small, with ankylosis of the proximal interphalangeal joint.

In the several forms of calcinosis and of ossifying myositis there is, as in the heterotopic bone formation, no demonstrable alteration in calcium metabolism. Laboratory studies are, therefore, useless in differentiation of these diseases. In contradistinction are the cases of metastatic calcification occurring in primary hyperparathyroidism or in renal rickets, with elevation of the blood calcium, lowering of the blood phosphorus, and increased urinary excretion of calcium.

The prognosis in heterotopic bone formation is necessarily uncertain, as none of the few case reports includes a long follow-up period. Consideration of the nature of the tissue changes suggests nonrecurrence, though some new lesions may be expected to develop after removal of earlier ones.

It is proposed to excise the plaques remaining in our patient and such additional ones as may arise subsequently in the belief that there will be no recurrence.

SUMMARY

Heterotopic formation of mature bone within the deeper layers of dermis, subcutaneous tissue, and muscle appears to be a rare malformation of segmental distribution occurring in young children. Simple excision is employed in treatment with apparent curative results. To the three cases found in the literature a fourth has been added.

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PRENATAL AURICULAR FLUTTER

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AURICULAR flutter is rarely noted in juvenile heart disease and actual prenatal arrhythmia with later demonstration of true auricular flutter has rarely been reported. Carr and McClure[1] noted fetal cardiac irregularity during the last month of gestation. Electrocardiographic proof of auricular flutter was given about twenty-six hours after the birth of the infant. Rhythm and rate returned to normal on the tenth neonatal day.

Sherman and Schless[2] reported upon findings in a 3-month-old male infant with occasional cyanosis and syncope. During the eighth gestational month, the rate was too rapid to count, although on one occasion a rate of 190 beats per minute was found. Electrocardiographic verification led to treatment with tincture of digitalis and restoration of normal rate and rhythm. The authors concluded that maturity of the conduction bundle established the normal mechanism.

D. Mc. was born on July 24, 1947, by classical cesarean section. Dr. Ross E. Griffith furnished the following obstetrical record:

Date	*Fetal Heart*
May 2, 1947	Rate, 156 beats per minute
June 6, 1947	Irregular
June 30, 1947	Rate, 208 beats per minute
July 5, 1947	Very rapid and irregular
July 12, 1947	Irregular: rate, 180 per minute
July 21, 1947	Irregular: rate, 136 per minute

The mother of the patient, a 41-year-old gravida v, para v, began to have profuse vaginal bleeding on the morning of July 24, 1947. An x-ray of the abdomen led to the finding of placenta previa. The health of the patient had been excellent during her entire pregnancy.

The infant was 51 cm. long and weighed 7 pounds, 13 ounces. Examination was entirely negative except for moderate cardiac enlargement and cardiac rate of 240. There was an inconstant, faint, systolic, precordial murmur. Transitory arrhythmia and cardiac rate of 150 to 160 beats per minute were noted. The infant was apathetic and nursed poorly. At no time was there evidence of congestive failure until on July 28 when definite sclerema was noted involving both thighs, particularly on the lateral aspect. Sclerema neonatorum has been held to be indicative of impaired circulation.

An attempt was made to stop the arrhythmia through vagal pressure but this proved unsuccessful. On August 4, quinidine sulfate was given in dosage of ¼ grain every four hours. The heart rate dropped to 112 to 120 per minute but the baby began to vomit feedings and to lose weight. The quinidine was stopped and within eighteen hours the heart rate was again over 200 beats per minute.

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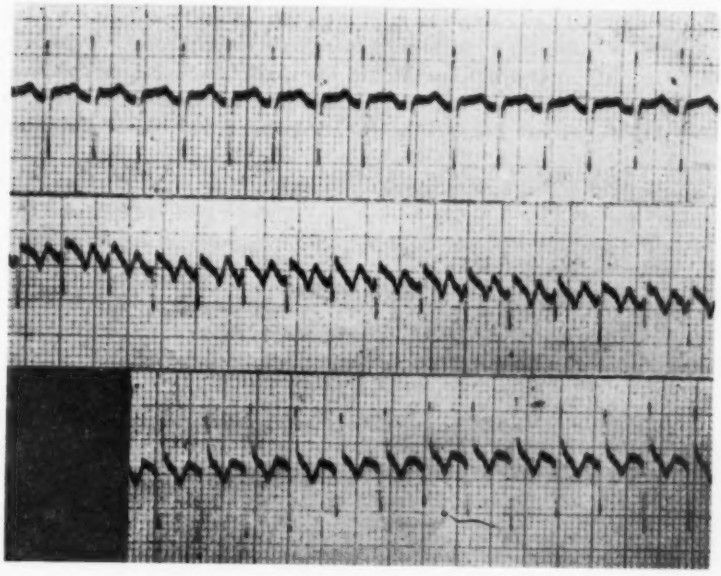

Fig. 1.—Electrocardiogram taken on July 30, 1947, showing auricular flutter with 2:1 conduction ratio in the limb leads.

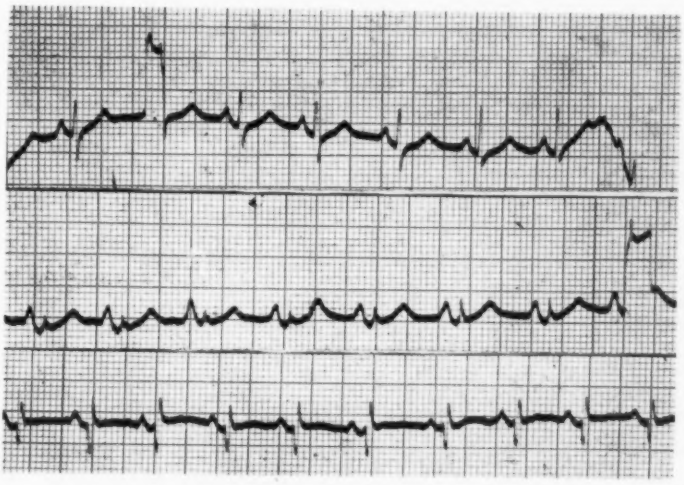

Fig. 2.—Electrocardiogram taken on Nov. 26, 1947, showing a sinus rhythm.

On August 15, Crystodigin (Eli Lilly Company) was given. An ampule of this preparation (1 c.c. containing 0.2 mg.) was diluted to 20 c.c. with sterile water and one teaspoonful (0.04 mg.) was given every six hours. Within thirty-six hours after the medication was begun the rhythm was normal and the heart rate was 120 to 128 beats per minute. The Crystodigin was given for three full days and then stopped. The weight of the infant began to increase normally. At the time he was 3½ months old, the baby weighed 16 pounds. The murmur could no longer be heard and cardiac size was normal. The infant weighed 23½ pounds and was 30½ inches long when he was 9 months old. Physical examination was entirely normal. There was no evidence of heart disease. The sclerema had disappeared.

SUMMARY

A case of prenatal auricular flutter (apparently the third reported) is presented. Therapy with quinidine sulfate proved effective but toxicity led to its withdrawal. Crystodigin therapy established a cure. It has been stated that the large diphasic QRS complexes in the first curve and tall P waves in the second curve are suggestive of congenital heart disease. Observation of the patient will continue although all factors involved point to the fact that a complete state of normality has been established.

The author expresses his appreciation to Drs. I. H. Zitman, Chicago, Ill., and E. Blatt, Indianapolis, Ind., for their electrocardiographic interpretations and to Dr. Ross E. Griffith, Indianapolis, Ind., for use of his records and for his deep interest in this study.

The Eli Lilly and Company, Indianapolis, Ind., furnished the Crystodigin.

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EMBRYONAL ADENOCARCINOMA OF THE TESTICLE IN A THREE-YEAR-OLD CHILD: REPORT OF A CASE

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CARCINOMA of the testicle in childhood is a rare condition, but a review of the literature indicates a frequency sufficient to make one suspect the diagnosis when a rapidly growing, firm, nontransilluminable mass is discovered in the scrotum of an infant or child.

Dean[1] reported a series of 500 cases of testicular teratomas in all ages. Eight of these occurred in children up to the age of 14 years, an incidence of 1.6 per cent. Paget[2] noted that tumors of the testis constitute 2.8 per cent of all tumors in infants.

Julien,[3] in a treatise on tumors of the testis in children, collected 137 cases. He noted that the incidence is highest during the first three years of life, and declines toward puberty. Kutzmann and others,[4] in a review of the literature, quote Steffen and Gerhardt who found that tumors of the testis occur chiefly in infancy, gradually diminishing in frequency in the second, third, and fourth years.

Practically all testicular tumors in infants are mixed or teratomatous, and the so-called seminoma is exceedingly rare. Chevassu[5] noted that five of 61 cases of teratomata occurred in children, whereas in a group of 59 such tumors there were no cases of seminoma in children. Dean[1] stated that, histologically, tumors of the testis in children are similar to those in adults. The bulk of these tumors consists of highly anaplastic embryonal cells. Adult structures with much greater cellular differentiation are also present.

CASE REPORT

A 3-year-old white male was admitted to Sarah Morris Hospital on July 30, 1947, with acute respiratory distress, characterized by wheezing, obstructed breathing, and elevated temperature. Physical examination and roentgenograms confirmed the diagnosis of bronchopneumonia. The respiratory symptoms responded promptly to medical management.

It had never been noted prior to admission that there were any genital abnormalities. It was discovered in the course of the admission physical examination that the right testicle was four times larger than the left. It was insensitive, nodular, firm, and did not transilluminate. The right epididymis and vas deferens were normal. There was no lymph gland enlargement. The left testicle was normal.

A clinical diagnosis of tumor of the right testis was made, and urologic consultation was requested. The patient was seen by Dr. Irving J. Shapiro, who concurred in the diagnosis and advised orchidectomy.

On Aug. 5, 1947, a right orchidectomy was performed. The postoperative course was uneventful. The dressings were changed and the sutures removed on the fourth postoperative day. The wound healed by primary intention. The patient was discharged on Aug. 9, 1947, and returned to his home in another state where intensive radiation therapy was given.

From the Sarah Morris Hospital, and the department of urology, Michael Reese Hospital, pediatric service of Dr. Philip Rosenblum.

Pathologic Report.—The specimen consisted of a testicle including the epididymis. The entire specimen measured 2 × 2 × 1.5 cm. The tunica vaginalis as well as the mesothelial covering of the epididymis and portion of the vas were smooth, gray, and glistening. The testis was deformed. On section, it was occupied almost entirely by a soft tumor which presented a pleomorphic appearance. Some portions were red, others bright yellow. The latter appeared as islands which were somewhat more elevated than the surrounding zones. The tumor occupied the entire testis except for a thin rim at the upper pole. Tumor could not be noted in the epididymis, tunica vaginalis, or any other surrounding tissue. The epididymis and vas revealed no gross changes.

Fig. 1.

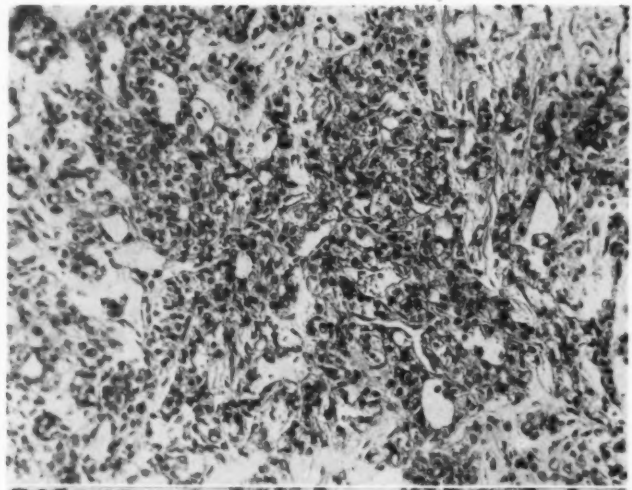

Fig. 2.

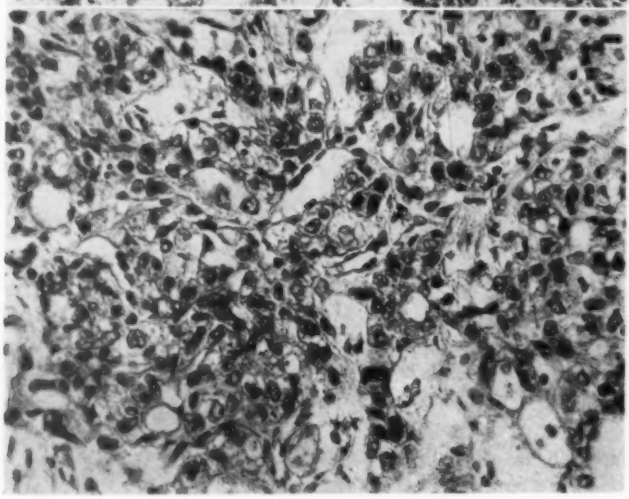

Fig. 1.—Photomicrograph of testicular tumor, low power.
Fig. 2.—Testicular tumor, high power.

Microscopic appearance is represented in Figs. 1 and 2. The sections consist of tumor cells arranged in masses or pseudoglandular formations, lying in a loose stroma. The cells are large and differ markedly in size and shape. The nuclei present a dense nuclear membrane but relatively scant chromatin material, and one or two prominent nucleoli. There are numerous typical and atypical mitotic figures. The cytoplasm is copious and clear or vacuolated. The stroma consists of loosely arranged fibroblasts and numerous dilated capillaries.

Pathologic Diagnosis: Embryonal adenocarcinoma of the testis.

SUMMARY

A case of carcinoma of the testis in a 3-year-old child is presented together with a brief review of the literature as to incidence and types of carcinoma of the testis in children.

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Erratum

In the article entitled "Generalized Vaccinia" on page 281 of the September, 1948, issue of THE JOURNAL, the name of the second author, Dr. Philip Hedrick, has been misspelled.

Clinical Conference

CONFERENCE AT THE ST. LOUIS CHILDREN'S HOSPITAL

JULY 30, 1948

ALEXIS F. HARTMANN, M.D., CHIEF-OF-STAFF

Case 1. Ovarian Tumor

DR. GERALD HUGHES.—The first case this morning is that of M. R., a 7-month-old white girl who was admitted to the St. Louis City Hospital on July 17, 1948, with the following history (which, as it turned out, proved more confusing than helpful):

The infant had been in good health until May 14, 1948, when, following the ingestion of some applesauce, she developed cramping abdominal pain, some fever, and passed several loose stools, one of which was blood-streaked. She was seen by a local physician, who advised the parents that the infant had an ear infection and gave her an injection of penicillin.

The next morning she seemed perfectly well again and remained so until July 15, 1948, when, following the ingestion of pears from a freshly opened can, she again developed cramping abdominal pain. She was very irritable and vomited once that evening and again the following morning. Later that morning she developed a fever and during the day had five bowel movements.

She was seen in the Receiving Room of the St. Louis City Hospital on the evening of July 16. At that time physical examination was nonrevealing except for some fever and irritability. The parents were told to omit all feedings for twelve hours and to bring the infant back the following day if she showed no improvement.

Feedings were resumed on the morning of July 17, and all were retained. The infant had one normal bowel movement that morning. However, the complaints of fever, irritability, and cramping abdominal pain persisted, and, in addition, the parents noted that her abdomen seemed more full than usual. She was brought back to the hospital on the afternoon of July 17.

At that time physical examination revealed a pale but well-developed and well-nourished infant who was quite irritable and appeared acutely ill. The abdomen was distended and there was generalized tenderness and voluntary muscle guard. No organs or masses were palpated at that time. Bowel sounds were hypoactive. Rectal examination revealed no tenderness or masses. The remainder of the physical examination was not abnormal except for the left tympanic membrane, which was thick and dull.

The infant was admitted to the hospital with the diagnosis of possible acute appendicitis.

Laboratory examination revealed the urine to be normal. The hemoglobin was 7.1 Gm. The white blood cell count was 18,800, with a marked left shift. Blood Kahn was negative.

A diagnostic abdominal paracentesis was performed in the right flank. A few drops of thin, bloody fluid were obtained, but it was felt that this fluid had not been obtained from the abdominal cavity. Smear of this fluid revealed no organisms, and a culture reported later revealed no growth.

The infant was given a transfusion of whole blood and started on penicillin, streptomycin, and sulfadiazine subcutaneously. A small enema was given with the return of soft, yellow stool. Wangensteen suction was begun.

The following morning, July 18, the infant's abdomen seemed less distended and was soft to palpation when she was quiet. No organs or masses were palpated.

On the morning of July 19 vaginal bleeding occurred, and drew our attention again to the presence of mild hypertrophy of the breasts and an excess of pubic hair, both of which had been observed but not considered significant. Vaginal examination revealed rugae increased in number and hypertrophied with bloody fluid seen coming through the cervix.

That afternoon, under anesthesia, a mass was easily felt in the right lower quadrant. Upon opening the abdomen a mass approximately 12 × 15 cm. in size was found lying in the right lower quadrant of the abdomen but attached to a pedicle extending to the left lower quadrant. It was hemorrhagic and necrotic and was attached to the left Fallopian tube, which also was greatly distended and hemorrhagic. The mass was twisted three times on its pedicle. The right ovary and adnexa and the uterus all seemed to be normal.

Histologic examination of the mass removed has so far been unsatisfactory because of the amount of autolysis which took place. A diagnosis of cystic tumor of the left ovary with hemorrhage and necrosis was made.

Postoperative course was uneventful except for a transitory elevation of temperature on the second postoperative day and the passage of one tarry stool on the third postoperative day. The infant was discharged from the hospital on the eleventh postoperative day.

DR. DON THURSTON.—This infant presented a somewhat difficult problem during the first forty-eight hours of hospitalization in that not only was the examination difficult, but its results were unsatisfactory. At the time of admission, with the evidence of impending shock and a blood picture suggesting the loss of blood and the presence of acute infection, we had difficulty in explaining all of the symptoms and signs on the basis of a single disease. The possibility that we were dealing with a surgical abdomen was uppermost in our minds. The patient's condition seemed too critical to tolerate an exploratory surgical procedure, and we felt that all we could do was to administer parenteral fluids and blood. The history of the onset of symptoms shortly after the ingestion of food suggested the possibility of food poisoning due either to preformed toxins or to bacterial invasion. The symptms of severe food poisoning are usually dramatic and are characterized by severe nausea, vomiting, abdominal pain, acute prostration, and diarrhea, with profuse sweating, hypotension, and shock, and, in the case of botulism, there is the curare-like action of the poison on the motor nerves and voluntary muscles. This child, however, had very little diarrhea or vomiting and no evidence of neurological changes.

With the persistence of the picture and with no evidence of infection elsewhere, it was felt advisable to attempt an abdominal paracentesis. This type of aspiration is done carefully with a small needle. The abdominal cavity is entered laterally with the bevel up, and mild suction is applied. Any material obtained is smeared on a sterile slide and stained. The remainder is cultured. By this means it is possible to differentiate primary from secondary peritonitis. The symptoms and physical findings in this infant were compatible with either diagnosis.

Other surgical conditions considered were: congenital anomalies with partial obstruction, intussusception, mesenteric lymphadenitis, and urinary tract infection, all of which conditions seemed to be ruled out on the basis of history and physical findings and the course while under observation.

At this point a review of the history again revealed a small point—that of recurrent but persisting breast enlargement. A direct examination of the genitalia revealed a definite but slight increase in the size of the labia and the presence of hair which was definitely unusual for this age group. On the third hospital day the infant had vaginal bleeding, sudden in onset and moderate in amount, of a serosanguinous nature. A smear of this material revealed no leucocytes but large polygonal cells with some evidence of nuclear degeneration. Vaginal examination with a speculum proved that the blood was coming from the cervix. The vaginal mucosa was definitely thickened with increased folds. The feeling of the observers was that we were dealing with a menstrual type of bleeding. With the child's condition improved, an exploratory laparotomy was done. At the time of operation and with the infant under anesthesia, a definite globular mass was both visible and palpable in the right lower quadrant. The preoperative diagnosis of ovarian tumor seemed to be correct, and on opening the abdominal cavity the diagnosis was confirmed.

In reviewing the cases published, the unusual feature in this case is the onset of menstrual bleeding following the torsion of the pediculated tumor. In recent years the effect of estrogens on the female human being has been widely investigated, and it is interesting to note that in this case, even with evidence of precocity, there was no bleeding until torsion of the tumor interfered with the blood supply. After experimental therapy with estrogen has been stopped, it is usually five to seven days before menstrual bleeding takes place. This concurs. Also, the vaginal thickening, breast enlargement, and some increase in size of the labia are the normal effects of estrogen in the prepubertal, castrated female. The microscopic sections are difficult to evaluate as to the type of tumor, because of autolysis. There are, however, two types of tumors that give rise to this type of precocity, the granulosa cell and the thecoma or thecal cell tumor. The manifestations in both are due to excess estrogen formation, and differential diagnosis is made microscopically. From the cases reported the prognosis seems good, but recurrences have occurred.

DR. PETER HEINBECKER.—I wish to present a case we had a few months ago. The child, 1½ years of age, was admitted extremely ill. The chief positive findings were those referable to the general appearance and to the abdomen, which was greatly distended. It was felt that the distention was due to fluid.

within which a tumor probably was located. A needle was inserted and some chocolate-colored fluid obtained. The child had prominent breasts and pubic hair was present; the labia were somewhat enlarged; the clitoris was not enlarged. The child looked older than her age and the eyebrows and hair were thick.

At operation there was found a large, right-sided, ovarian cyst with the pedicle partly twisted. The pelvic structures on the left side were normal. The uterus was slightly enlarged.

On microscopic section a typical thecal cell tumor was diagnosed. There were many small spaces lined by secretory cells.

The child has not been seen since the time of discharge. It is expected that she will show a recession of the signs indicating an excess estrogen secretion.

DR. ALEXIS F. HARTMANN.—Dr. Thurston, is it not fair to state that as soon as more or less emergency treatment had been rendered this child (fluid administration and blood administration) the over-all picture then suggested a serious intra-abdominal condition that one would ordinarily associate with a surgical lesion sometimes found with appendicitis, especially with localized abscess formation, or a Meckel's diverticulum with peritonitis or abscess formation? Having reached the point where one had to consider the child as requiring surgical intervention regardless of what might be found, ought not the baby to have been explored without further delay? Do either of you, Dr. Veeder and Dr. Cooke, remember any child in whom a diagnosis was not made sufficiently early in the case of a twisted ovarian pedicle or any other ovarian cyst with hemorrhage into it? What should we expect to happen if a diagnosis is not made and proper surgery performed?

DR. HEINBECKER.—Under those circumstances invasion of the tumor by organisms may lead to peritonitis. An aseptic peritonitis only may occur.

DR. HARTMANN:—The picture of a pelvic abscess?

DR. HEINBECKER.—Diffuse pelvic and abdominal peritonitis.

I should have mentioned that in this case withdrawal bleeding also occurred on the third day following removal of the tumor. The bleeding from the uterus lasted for three or four days.

DR. HARTMANN.—Dr. Thurston, would you regard this vaginal bleeding as similar to the bleeding seen in newborn babies as the result of deprivation of estrogen?

DR. THURSTON.—Yes, quite similar in character. This child had menstrual bleeding on the sixth day.

DR. HARTMANN.—However, the breast enlargement seems to be different from that in newborn babies. The breasts are not engorged but are definitely enlarged. There is protrusion, not retraction, of the nipples.

If you had not found the tumor, would you have been much impressed by the pubic hair or breast enlargement in this baby?

DR. THURSTON.—Yes, I was impressed with the pubic hair and pointed it out on several occasions. It seemed too much for this age. It was quite sug-

gestive of a patient of Dr. Hartmann's and suggestive also of a patient with endocrine dysfunction—the dwarf—in which definite increase in pubic hair was seen. There also seemed to be some pigmentation of the skin which was not due to sunshine, because it has faded a little too fast.

DR. HARTMANN.—Do you think you should have been able to feel this mass rectally?

DR. THURSTON.—Under anesthesia, yes, but not without anesthesia. Numerous rectal examinations were made, but no mass could be felt.

DR. PARK J. WHITE.—There is much in this case to attract attention to the genital system. Did you find any trouble with the appendix? I have cited previously a patient with an acute appendix in addition to an ovarian cyst of this type. Which came first? The acute appendix or the ovarian cyst? Undoubtedly, the ovarian cyst came first, but the appendix was inflamed as well.

DR. READ BOLES.—The appendix in this case was not explored.

Cases 2 and 3. Esophageal Stenosis Following Ingestion of Lye

Case 2

DR. RALPH LUCE.—This patient, H. B., is a 2-year-old Negro girl who entered Children's Hospital seven weeks ago. She had been well until one week before entry when she drank a glass of milk containing two tablespoonfuls of lye. She suffered severe burns of the mouth and was taken to another hospital for four days where she received penicillin and parenteral fluids. She was able to swallow only fluids during the three days prior to entry to this hospital.

With a barium swallow a constriction was seen in the esophagus about one or two inches above the stomach. Attempts to pass a weighted string into the stomach were unsuccessful. An esophagoscopy was then done, which revealed a slitlike stricture 22 cm. from the central incisors. Gradually less food could be taken orally, and parenteral feedings were necessary during the third week in the hospital.

Three weeks after entry and four weeks after the original injury the esophageal stricture with the segment of esophagus distal to it was excised and an esophagogastrostomy and vagotomy were performed. The immediate postoperative course was uneventful. When oral feedings were resumed, the patient took them without difficulty in swallowing and without vomiting. Eighteen days after the operation she began to refuse much of her feedings. This seemed to be corrected when a more palatable diet was offered; however, the past four days she has again refused a large part of her food. She has regurgitated a small amount twice during this time.

A barium swallow done six days ago devealed a functioning esophagogastrostomy.

This x-ray (Fig. 1) of the barium swallow taken prior to operation demonstrates a constriction of the lumen in the distal 3 to 4 cm. of the esophagus with a dilatation of the esophagus superior to the stricture. The barium mixture is seen to pass through the stricture in a trickle.

The barium swallow done last week (Fig. 2) shows prompt deglutition, barium passing promptly through the artificial stoma into the stomach. There is eventration of the diaphragm, so that the stomach is displaced upward.

Fig. 1.

Dr. Alexis Hartmann.—I think this is our first child to be operated on with the bringing up of the stomach into the thorax and anastomosis to the esophagus. It is of interest to consider that we have essentially created a condition which we sometimes think is necessary to correct surgically—a diaphragmatic hernia with the stomach in the thorax. We recall, too, that in the last year or so Dr. Fields reported on four very intertesting children, each born with a congenitally short esophagus, who later began to regurgitate food, often mixed with blood. Are we going to have trouble of that sort with this operation, which otherwise seems almost perfect? You remember that the piece of esophagus resected and shown to us a week or two ago was very fibrous. Everyone agreed that it could never have been dilated successfully. Because a piece of the vagus nerve was resected in this child, the danger of such peptic ulceration is probably considerably minimized. The results in treatment of peptic ulcers suggest that such vagotomy is of considerable value.

DR. ROBERT SCOTT.—What period of time was there between the swallowing of the lye and the operation?

DR. LUCE.—Four weeks.

DR. SCOTT.—Is it possible that that operation was performed a little soon after ingestion of the lye and that stricture migh have developed higher up after operation?

DR. PAUL J. ZENTAY.—That is not likely after four weeks. It has been demonstrated by x-ray that there is no other stricture.

Fig. 2.

DR. HARTMANN.—There is nothing to indicate stricture in the upper portion, and it is amazing to see how much scar formed in the lower segment in the four weeks following the injury. If some constriction should still develop in the upper portion, it ought not to be difficult to dilate from above.

DR. SCOTT.—A word about vagotomy. I saw some adults in San Diego who had this done for recurrent peptic ulcers, and they developed symptoms of diarrhea, etc. following vagotomy. It is not an entirely benign procedure.

DR. HARTMANN.—In one of our infants born with esophageal atresia, following esophageal anastomosis the vagotomy syndrome made its appearance and resulted in marked gastric atony and much regurgitation which finally led to dehydration and alkalosis. In that child Urecholine seemed to be of value in stimulating gastric peristalsis. Eventually this child recovered.

DR. ZENTAY.—How much vagus nerve was resected?

DR. HARTMANN.—About 4 cm.

Case 3

DR. C. W. DAESCHNER.—D. E., a 34-month-old white boy, was first admitted to Children's Hospital on July 30, 1947, at the age of 21 months because of inability to swallow. The mother stated that in September, 1946 (twenty-two months ago), the patient swallowed some lye solution, resulting in burns of the mouth and esophagus. He was hospitalized for three days and given penicillin. No other therapy was given. After healing, the patient was able to swallow only strained foods and liquids, so he was hospitalized again and the physician said that there was pressure on the esophagus but that it was too low to stretch the esophagus. The patient was transfused and dismissed. In the interim he has remained on a liquid diet, gained weight, and done well until three days prior to the original admission to Children's Hospital, when he developed a cough and with it inability to retain any solid food and only very small portions of water. Food would be swallowed and then regurgitated immediately.

On admission, the patient was thin, pale, dehydrated, and febrile (39° C.) with mild acidosis and acute pharyngitis. As soon as the physical condition improved, a dilatation of the esophagus was done under anesthesia. A stricture was visualized 13 cm. from the incisor teeth. Bougie dilators were inserted up to No. 16. Following this procedure, the patient's ability to swallow was much improved and milk and water were then taken comparatively well. Dilatation was repeated three days later to a No. 20 bougie which passed with some difficulty. After this therapy, subcutaneous fluids could be omitted, and the boy could handle a regular infant diet quite well. Dilatation was repeated four days later, this time to a No. 20, and progress was so good that it was decided that dilatation could be carried out only once weekly. He was dilated for the fourth time one week later. At this time a No. 4 bronchoscope was passed through the first stricture down to the second series of strictures and through these. The patient was then discharged on a regular diet to return in two weeks.

Two weeks later the patient was readmitted in good condition and was able to swallow a regular infant diet (milk, Pablum, orange juice, water, etc.). This time a No. 4 bronchoscope and a No. 9 bougie were passed through both strictures. Results were good, and the patient was dismissed to return in three weeks for dilatation.

At the time of readmission three weeks later, the child was still on a regular diet, now including cereals, crushed spaghetti, strained vegetables, and all liquids. The patient was dilated as before and dismissed in good condition.

He was readmitted (this time to McMillan Hospital) three weeks later and dilated as before with good results and told to return in one month.

He was readmitted in December and this time dilated to a 5 mm. bronchoscope, and the second stricture was described as spiral in type. He was discharged improved.

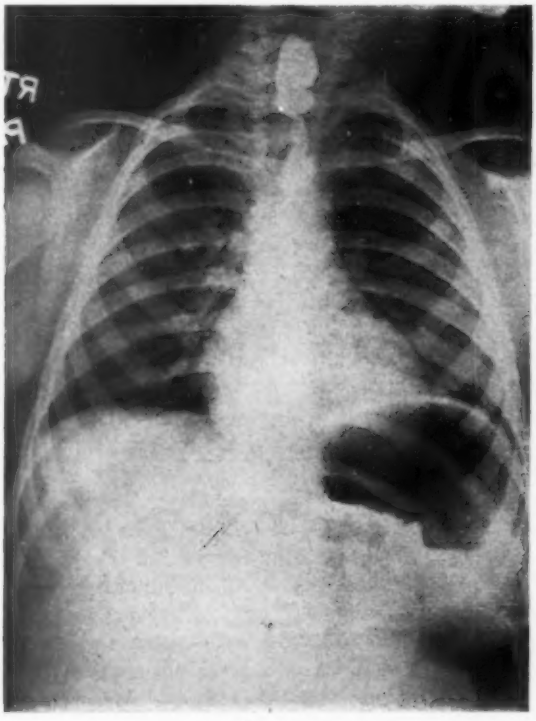

Fig. 3.

Five months later he returned to Children's Hospital with the story that he could not even swallow his own saliva for the past two days, but after hospitalization ability to take fluids orally returned spontaneously. When the patient was hydrated, esophagoscopy was done with a No. 6 scope passed to a pinpoint stricture 16 cm. below the incisors, and bougies up to No. 16, were passed through the stricture down to a 50 cm. level. Repeated attempts were then made to allow passage of a shot on a string, but each time the shot lodged at the stricture.

On June 29, 1948, the patient was esophagoscoped, a 35 Jackson scope being passed without difficulty through the stricture at 14 cm. below the upper incisors. The stricture was described as firm, annular, with a 3 to 4 mm. lumen, and the mucous membrane for 1½ cm. above the stricture was pale and scarred.

Several radiographic studies of this patient have been made over the period of his stay at Children's Hospital. These are all similar, so that the most recent anteroposterior and lateral views (Figs. 3 and 4) taken with a thick barium swallow serve to illustrate the esophageal deformities. The first stricture, which represents the one described as 14 cm. from the incisors, is visualized just below the dilated portion of the esophagus and just above the manubrium. It is about ½ cm. in diameter. The second stricture is visualized approximately 2 cm. lower and, in the lateral view, is seen to be 4 to 6 cm. long and with a 2 to 3 mm. lumen. No other evidence of stricture or anomaly of the esophagus is noted.

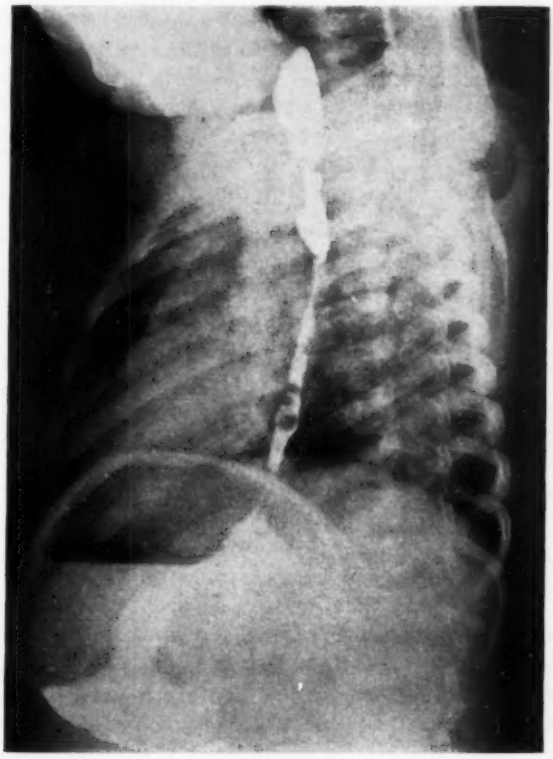

Fig. 4.

DR. HARTMANN.—This is a problem because the stricture begins high, is multiple, and involves the larger portion of the esophagus. It would seem fairly obvious that the relatively simple operation which had been performed in the girl, bringing the stomach up and anastomosing to the good upper part of the esophagus, would not work well here because too little good upper esophagus is left, and also it would seem that the operation described to us a few weeks ago by Drs. Burford and Bricker, of making a new upper esophagus by

means of a skin tube, would in itself not suffice. It would solve the difficulty of the upper esophagus but not the lower esophagus. So this child would have to have both operations, the tube for the upper and the anastomosis for the lower portion. This child, while in excellent condition, is getting worse. He has lost several pounds in the last few weeks and takes longer to eat. Many unsuccesful attempts have been made to dilate from above. Now the question is: shall we go ahead and do with him what we have usually done? Shall we do gastrostomy and then make further attempts to pass a string, so that dilatation with bougies would be possible? Recently it has been emphasized that once you do gastrostomy, you immobilize the stomach and prevent bringing it up any distance into the chest for anastomotic procedures. That knowledge has made us hold off until now. Are we correct in concluding that our experiences and results with gastrostomy and retrograde dilatation in the past, have been so poor that we should discard that procedure? Some think so, and some do not. Dr. Webb has gone over all of our cases and will give you a picture of what has happened. It is my hope that Dr. Webb's analysis will make it easy for us to say whether we should go back to our old method with this child.

DR. BAILEY WEBB.—You have just heard presented the cases of two children who swallowed lye. They are both about 2 years of age and were taken to hospitals as soon as the accidents were discovered. Early treatment was conservative, and the children were not seen here until after strictures had formed. The first child had a low stricture and was treated surgically. The problem of the management of this second child with multiple strictures prompted us to review the records of our previous cases and their outcome.

Since 1926, there have been thirty-eight patients with lye burn of the mouth and esophagus admitted to St. Louis Children's Hospital, twenty-nine white and nine Negro children. Although the ages varied from 5½ months to 7 years, the majority of these patients were between 1 and 3 years of age. Nine of the children were seen here less than forty-eight hours after the accident, and twenty-nine had some evidence of stricture at the time of entry. The incidence of strictures was higher after the ingestion of dissolved lye, but nine cases of stricture developed from taking powdered lye.

In all patients there was an initial anorexia, and many were never able to take solids well. The usual story is that after the mouth heals, swallowing improves, but this is followed by increasing dysphagia, first for solids and then for liquids. In most cases it becomes a serious problem in from 2 to 4 weeks, but in one case the time was less than one week and in three cases, more than two months. There were slightly more burns in the upper third of the esophagus than the middle and lower thirds.

In ruling out the diagnosis of stricture, unless thick barium is used the barium swallow may be misleading. On my initial examination of the first child presented today, I failed to see a stricture when using thin barium, and examination of the records shows that to have been the experience of the pediatrician and roentgenologist on occasion.

The treatment of these patients depends on whether or not they are seen before or after the stricture has formed. It is pathetic to note that at least thirty of the patients in our series were seen by a physician within forty-eight hours of the ingestion of the lye and that most of the parents were instructed to give the child some local mouth care and told that all would be well. Several of the parents reported that the children spat out the lye and that the doctor felt that only the mouth was burned at the time.

Of the nine children seen at the St. Louis Children's Hospital early, only two developed strictures. One was the first patient, in 1926, and the other a recent 5-year-old boy who drank a very caustic boiler compound.

The routine early treatment consists of frequent sips of orange juice for the first forty-eight hours. Beginning at the end of this time, mercury-filled bougies are passed daily, starting with the 14 French and rapidly increasing the size and length of time of dilatation until on the fourth day a 30 French bougie is left in place for thirty minutes. Dilatation with the 30 French is thus continued daily for at least two weeks, every other day for two weeks, twice a week for two months, once a week for two months, every other week for two months, and monthly for five months. Strangely enough, if the procedure is done with firmness and sympathy, it is tolerated well. Blind dilatation from above is stopped if evidence of stricture occurs, and other methods of treatment are used.

After strictures have formed, the patients usually have been treated by dilatation from above under direct vision or by gastrostomy with retrograde dilatation. There have been seven patients treated by the first method, one the patient under discussion. Three of these have been seen one to ten years after the treatment with some complaint of dysphagia; three have not been heard from, and one died in 1934 from perforation of the esophagus by an esophagoscope. Twenty patients have been treated by the method of retrograde dilatation. Eight of the patients have been followed until the gastrostomies were closed, and although there was a latent period between the last dilatation and the closure of the gastrostomy, none reported any dysphagia at the time of the closure, and there is a follow-up on only one, who reports occasional difficulty with the swallowing of solids. Seven are still being followed in ENT Clinic and have their gastrostomies still open. One child died of measles and pneumonia, and we have no information at present on four others. Though the gastrostomies were usually closed in from one to three years, one child has had one for five years. The thing that impressed me most was the technical difficulty the ENT man encountered in passing the string if the stricture were very small. Usually three weeks or more were required for this after gastrostomy, and in one case it took three years.

Two patients have been treated surgically, the child presented today and one child for whom Dr. J. B. Brown constructed an external skin-lined tube in 1938. This child was operated on two years after his stricture had become complete. Dr. Brown has no follow-up on this boy.

As stated above, we have had only two deaths, one from mediastinitis before the days of chemotherapy and one from an intercurrent infection.

Considering the numerous esophagoscopies, it is a tribute to the ENT staff that there have been only two patients with perforation, the last one of whom made an uneventful recovery without signs of mediastinitis, due to vigorous coverage with antibiotics and sulfonamides as soon as perforation was discovered. Dr. Stutsman will discuss the treatment of lye burns from an ENT standpoint. We regret that Dr. Burford is on vacation and cannot discuss the surgical treatment.

DR. A. C. STUTSMAN.—I would like to say something about the method of treatment of lye strictures months after the stricture has formed. I would like to emphasize the importance, first, of maintaining the fluid intake of the patient and of doing something about the nutritional status of that patient. That is often a problem and must be attended promptly once the child comes in for observation. The next thing is the diagnosis, and this can be established in two ways: (1) barium swallow, and (2) esophagoscopy. Certainly all patients should have esophagoscopy at the beginning of treatment to determine the amount of stricture and the location and character of the stricture. Once this is done, treatment may follow one of these courses: (1) Bouginage in the direct manner through the esophagoscope. This method is satisfactory in some cases. It is used extensively in some centers, and I think it depends to some extent on the number of strictures and how difficult the esophagoscopy is. I think it is the most dangerous of the methods. There were no cases of rupture by the retrograde method. The one rupture was by the direct method. If the case is such that the direct method is not considered satisfactory, then we use (2) retrograde bouginage. Gastrostomy is necessary in order to use this method of treatment, and serves a double purpose because many children are in a bad state of nutrition, and gastrostomy can be used to re-establish adequately the nutritional condition of the patient. So this method may be used for treatment of the general condition of the body and later for dilatation of the stricture. A string should be introduced into the esophagus and into the stomach as promptly as possible after the patient comes under observation. Much time is lost in getting the string down, and you heard what the varying periods of time required have been. Some of that is due to the fact that we have not been too diligent in trying to accomplish this and lose time. Every effort should be made to get the string down promptly. Lead shot has been mentioned as useful, but it is important to remember that it may serve as a foreign body and block the stricture. After gastrostomy is done and the child has recovered generally, nutrition is adequate, and the string down, bouginage can be started. This is fairly simple. A bougie is pulled through the gastrostomy up through the esophagus and mouth. We start with a small size and increase the size as we go on. The usual thing is to take two or three bougies through at one sitting if possible, the first serving as a test bougie. If it is too tight, we start over.

If retrograde dilatation is not successful, we consider (3) surgical procedures. The esophagus can be exposed at the location of the stricture and the surgeon can guide a filiform bougie through the stricture safely into the stomach

to permit a string to be pulled through. The location of the stricture has something to do with whether or not such surgical exposure would be a fairly safe procedure. It can be done in the upper third; the middle third might produce some danger; it can be done in the lower third. I should have mentioned before that esophagoscopy can be done in the usual way and then retrograde esophagoscopy can be done using an esophagoscope or cystoscope so as to pass the lower third of the esophagus and then from above and under biplane fluoroscopy a filiform bougie may sometimes be passed. All this requires much patience on the part of the physician and understanding on the part of the parents. One must endeavor to be patient with the parents too. It is a long, drawn-out procedure.

Dr. Paul Zentay.—I would like to say something about the problems presented here. Twenty-five years ago this fall the first patient in this country was treated with this preventive method by Dr. Wilburt Davison and myself at the Harriet Lane Hospital. This is the first time results obtained here have been summarized. Out of nine patients receiving proper early treatment, seven had no trouble at all. The other twenty-nine had to go through tortures, and you have heard what it means to treat them from above or below. The children coming to the hospital late were extremely emaciated and had other evidences of starvation. Today the problem is a public health problem, and there is no reason why the figures we have here should not be published, so similar tragedies will not occur again. The data should be made known to doctors. One important point in the first examination is that the fact that the child has no burn in the mouth is not significant. There may be a bad burn in the mouth and not much in the esophagus, or there may be nothing in the mouth and a very severe burn in the esophagus resulting in extreme stricture. It is very gratifying that our results are in harmony with those published almost thirty years ago.

Dr. Park White.—Dr. Webb said that in the first case treatment was conservative. She meant treatment was bad. The first patient did not appear at Homer G. Phillips Hospital. At Homer G. Phillips Hospital patients are tubed very quickly, and I think in the early days we were too much afraid of poking a tube into the mediastinum, and hence many patients were deprived of early treatment. At Homer G. Phillips Hospital, economic circumstances, etc., cause us to see many of these patients. The mothers work, and the children have access to lye.

Dr. Webb.—These bougies are not long enough for an adult. At City Hospital, Dr. Ogura had a rather disappointing experience in that he used them on an adult, and after a while a stricture formed. Fluoroscopy with the bougie in place showed that it reached just to the cardia where there was a stricture. On esophagoscopy, scars of the esophagus were seen above the stricture, but the lumen was adequate as far as the tube reached. These children are hard to manage with longtime therapy. They do not cooperate; they do not like to come back. If there is a gastrostomy tube in place, they are more willing to come back.

DR. HARTMANN.—Aside from its academic interest, Dr. Webb's analysis should help guide us in taking the right course at all stages of difficulty. Dr. Webb, have you also come to these conclusions: (1) that our own experiences, together with those already published, point overwhelmingly to the good results that can be obtained with little or no danger from early dilatation, so that every effort should be made to see that the strictures are dilated early; (2) that we should never be lured into a position of false security by being permitted to believe that only the mouth is burned or that the lye was spat out without having gone down to burn the esophagus; (3) that we have to be prepared for two types of failure: (a) stricture developing under treatment—two of ours showed that; (b) the development of stricture in a child with no treatment; (4) that we should be on the look-out for the type of case with injury confined to the lower third of the esophagus, as these are the ones that we should not want to overlook too long? In the others we can try the usual treatment, but this is not doing the best service to the child who has a very serious stricture in the lower part of the esophagus, for, if we are not successful with the usual treatment, it might be impossible to bring up the stomach to the esophagus for anastomosis. We want to get good visualization of the esophagus by the direct method or by the indirect method and feel strongly that thick barium has to be employed or a false conclusion may be reached. To satisfy my curiosity, was it a well-developed stricture that you failed to visualize?

DR. WEBB.—It was in the little girl. It was a well-developed stricture, but the child was hard to handle under the fluoroscope; she cried, and the barium fell through the stricture and could not be seen.

DR. HARTMANN.—It was a short stricture with a narrow lumen, but the material could get by, and did pass so rapidly that you failed to visualize it. With thicker barium, visualization is better; it goes through more slowly.

Also, we learned that in the short time of four weeks following injury very firm scarring can occur that would be hard to dilate. So, if we are on the lookout for only lower third involvement, fairly early operation of the type that the girl had, bringing the stomach up into the thorax, should be considered. In all other types fairly early gastrostomy with attempts to pass the string should be made. If we wait too long, nutrition fails, and it is hard to pass the string. If there is involvement of only the upper third, and gastrostomy and passage of the string and attempted dilatation have failed, then these may be screened out for the surgical tube method. As far as this patient is concerned, our feeling is that we should waste no more time and go ahead with gastrostomy with attempted passage of the string for retrograde dilatation. Dr. Zentay, do you also come to that conclusion?

DR. ZENTAY.—There is no question about it.

DR. ROBERT GARNER.—Dr. Stutsman, how soon is it safe to do esophagoscopy after swallowing lye?

DR. STUTSMAN.—It varies with the child. About a two- to three-week period would be moderately safe.

DR. GARNER.—Are you committing yourself to long-term treatment with mercury bougies? There will be certain cases where children would not have gotten lye into the esophagus. How would you tell which they were?

DR. STUTSMAN.—I think esophagoscopy and barium studies will tell that. Esophagoscopy should be done four to six weeks after it happens if there is some doubt as to the amount of damage to the esophagus.

DR. MIRIAN PENNOYER.—Regarding replacement of the upper third of the esophagus by a tube in certain selected cases, what happens as the child grows? Must we anticipate reoperation and substitution of a larger size tube in a few years?

DR. HARTMANN.—The method of reconstituting an upper esophagus in children has not yet been done, so I cannot answer that. In adults the procedure has been used in patients with carcinoma, and that has not allowed any long-time study of the situation.

Do you really believe, Dr. Stutsman, that if we went on the assumption that the esophagus had been injured and started on a dilatation program as outlined, then went along two or three weeks with no difficulty and wondered if we had to go through the whole program, that we could certainly find out by esophagoscopy if there had been injury?

DR. STUTSMAN.—I think you could to a reasonable degree. I would, however, keep the child under observation.

DR. HARTMANN.—In the second patient, the child swallowed boiler compound and developed stricture despite dilatation. Was esophagoscopy made at any stage, and what were the findings? Dr. Webb felt that at one stage we waited a little too long.

DR. WEBB.—Esophagoscopy was not done on that child until one month after the child had taken boiler compound, and we also began to run into trouble with dilatation from above. I wonder if our mistake was not that we dilated daily for two weeks, and then during the last two weeks when on an every-other-day schedule four days were skipped without dilatation. It was at that time that we first noted trouble.

DR. STUTSMAN.—Do you think that construction of a tube should be delayed until other methods have failed?

DR. HARTMANN.—Yes, because the tube is good only for upper strictures. In the cases with lower stricture you might not be doing the right thing in delaying anastomosis and attempting dilatation first.

To get back to Dr. Garner's question: Are you committing the child to a whole course of dilatation if you are not sure that burn has occurred? Dr. Garner, I would rather see fifty children go through dilatation unnecessarily than have one miss it who needs it, because results are so bad if that happens.

DR. WEBB.—I think prophylactic dilatation should be carried out for two months at least and then if no suspicion of stricture is present, diagnostic esophagoscopy should be done.

DR. HARTMANN.—Is it what you see through the esophagoscope or what you see as a result of barium or Lipiodol instillation that is diagnostic?

DR. STUTSMAN.—I believe esophagoscopy is diagnostic. You see an irregular lumen or evidence of scarring in some places through the esophagoscope as early as five to seven days.

DR. HARTMANN.—So then, if you saw scarring or an irregularity of the lumen, you would go ahead with dilatation.

Case 4. Tetanus

DR. JAMES MCNEIL.—J. G., an 11-year-old white boy, was admitted to the hospital on July 19, 1948, complaining of difficulty in opening his mouth and swallowing and of intermittent attacks of severe, generalized stiffness.

Five months prior to admission he sustained a compound fracture of the left tibia and fibula when struck by an automobile on a country road. He was treated with traction, casts, and penicillin, and the fracture healed uneventfully. He had no history of antitetanic serum or of other tetanus immunization. Nine days before admission his cast was removed, a small draining pressure sore was observed, and the cast was reapplied. No antitoxin was given.

Two days before admission he began complaining of difficulty in opening his jaws and swallowing and of pain through his shoulders and back, particularly when walking. Due to his abnormal gait associated with his fracture, it is difficult to determine if he had any disturbance in walking due to tetanus prior to the onset of generalized tetanic contracture. On the morning of admission, the patient started having intermittent attacks of opisthotonos, complete loss of voluntary muscle control, and moderate respiratory distress. These manifestations became progressively more severe, and it was noted by the parents that they could be precipitated by any ordinary stimulus such as jarring the bed, any sudden noise, or moving the patient.

Physical examination revealed a well-developed, well-nourished 11-year-old white boy who could not open his mouth over one centimeter. His speech was somewhat nasal in quality and difficult to understand. He had multiple skin lacerations over the right foot and leg, an old laceration surrounded by a ½ by 3 cm. area of reaction on the medial aspect of his right elbow, and two small, healed areas beneath his cast which may have been pressure sores. All cultures from these lesions were negative for *Clostridium tetani*. He was extremely restless; his abdomen remained boardlike between tetanic contractions, and, as noted by the parents, any ordinary stimulus precipitated an attack of rigidity.

Treatment consisted of a 70 mg. per kilogram dose of Avertin per rectum which brought about complete muscle relaxation. He was then given a total of 100,000 units of tetanus antitoxin, 50,000 units intramuscularly and 50,000 units intravenously. General precautionary measures such as darkening of the room, no visitors, minimal manipulation, and special duty nurses have been observed. He had been given nothing by mouth and maintained on 1,500 c.c. of intravenous fluids per day. Three hundred thousand units of Duracillin have

been given intramuscularly each day as prophylaxis against pulmonary complications. Sedation sufficient to keep the abdominal muscles relaxed has been maintained with approximately 80 mg. per kilogram of Avertin every four to six hours.

During the first four days in the hospital, the patient had repeated bilateral spontaneous epistaxis and had to be suctioned frequently to keep the respiratory passages open. On the fourth day he aspirated some blood and became very cyanotic. A tracheal catheter was passed, and a large amount of blood was aspirated from the trachea. During the next eight hours he had shifting breath sounds, frequent coughing, and more epistaxis. A tracheotomy was performed, and a large amount of blood was again aspirated from the trachea.

The patient has improved steadily since tracheotomy. He is now being sedated with sodium phenobarbital and a minimum of Avertin. For the past two days he has been fed by means of a stomach tube and is to be started on oral feedings tomorrow.

Dr. Jean V. Cooke.—This is the fifty-seventh patient with tetanus treated in this hospital, and since I had made an analysis of the previous cases, certain features are of interest to mention. The cases can be divided into two groups: (1) twenty-four patients admitted from 1916 to 1932, and (2) thirty-two from 1933 to 1947. Since 1933, we have used the current type of treatment with anesthesia with Avertin to be mentioned later. Previous to that time much less sedative was given, and the results were very unsatisfactory. Of the twenty-four patients treated from 1916 to 1932, twenty died, an 82.5 per cent mortality. In contrast, of the thirty-two patients seen since 1933, only eight have died, a 25 per cent mortality. Of this original group of cases in which there were only four recoveries in twenty-four cases, one patient who recovered was mildly affected and the other three severely, and all received 100,000 units or more of antitoxin. Of the twenty who died, only two received such large doses; the others averaged a dose of about 20,000 units. I do not mean to imply that the large dose of antitoxin was entirely responsible for the recovery or that death could be attributed to the smaller dose. Actually, five died four to twelve hours after admission; eight died the first day, four the second day, one on the third day, so that deaths of these earlier cases were fairly prompt. We believe in retrospect that some of these deaths could have been prevented by prompt, adequate sedation, since our present conception is that death in tetanus in the majority of cases is due to a convulsion or spasm of the respiratory muscles. If this can be prevented, there is a good chance that the disease may be prolonged until the tetanus toxin is oxidized and the stimulation of the muscles ceases.

The various portals of entry are of some interest. In certain cases no wound can be discovered, and it has been suggested that the portal of entry might be through the gastrointestinal tract, although this is rather speculative. In these fifty-six children, thirteen, about 20 per cent, had no demonstrable portal of entry. In the others, several different types of wound were found. The commonest was a laceration (twelve cases), puncture wound (ten cases), wound

from a splinter (seven cases), gunshot wound (six cases), two cases of tetanus neonatorum, one burn from a toy pistol, one following a compound fracture, one following ritualistic circumcision, one in a 9-month-old child following a cut on the lip after a fall out of bed, one following a puncture wound of the palate (the child fell with a stick in his mouth), one from a foreign body in the ear (a piece of coal). It is apparent that a variety of wounds have been followed by tetanus, many of them a small scratch or laceration, and in only a small percentage is it the typical punctured wound. Boys are more susceptble than girls in proportion of 2 to 1. By age, the largest group was in the second 5-year period (5 to 10 years) with twenty-six, while seventeen were under 5 years, and 13 from 10 to 14 years. The diagnosis was usually easily made as the classical signs of stiff muscles, trismus, etc., were usually present. In one child, however, the signs were those of severe, acute encephalitis, and the disease was unrecognized. So far as the incubation period is concerned, there is evidence that the patients suffer more severely the shorter the incubation period, it being assumed that the toxin formed in large amounts is absorbed rapidly and produces symptoms earlier. Actually we did find that most of the deaths occurred in children in whom the incubation period was less than a week, and those in whom it was longer than a week were less severe. Another point of some importance in prognosis is the duration of symptoms before the child is brought to the hospital. When the symptoms appear and progress very rapidly to the point of convulsion, the disease is much more serious than when slight stiffness of the muscles and trismus have been present several days before the patient comes to the hospital.

In about 1933 we started on the hypothesis that we should attempt to prevent convulsions by some powerful sedative, and since that time all the cases have been treated with Avertin except one, which was so mild that no sedative was necessary. Of the remaining thirty-one, eight were fatal, and in almost all of these children death apparently was due to bronchopneumonia, since, as might be expected, patients under such sedation have a tendency to develop pulmonary infection and aspiration pneumonia. Most of the fatal cases were treated before the sulfonamides and penicillin were available. Several children who were fed by gavage developed aspiration pneumonia and at least two died from pneumonia after the tetanus symptoms had subsided. It was apparent that the danger of aspiration could be minimized by giving nothing by mouth during Avertin sedation. Six of the eight deaths were apparently due to pulmonary infection. One child died in a convulsive spasm due to insufficient sedation. One child died two days after admission apparently from respiratory and circulatory failure; since the convulsions were controlled, there was no oversedation nor any sign of pneumonia. Two children have had tracheotomy as in the one here reported because of aspiration of blood from biting the tongue. One died from bronchopneumonia, and one recovered. We have had no deaths since 1944 and have reason to hope that the chief cause of death, bronchopneumonia, will now be greatly lessened by the use of sulfonamides and antibiotics.

DR. HARTMANN.—I would like to outline therapy given in the past. Here it is fairly easy to agree on principles of treatment; sometimes it is more difficult to carry out details of these principles which are called for. This child was tracheotomized, and I think we overlooked something important. As Dr. Cooke has outlined, it certainly has seemed, from results up to 1932 to the introduction of sulfonamide drugs and penicillin, that just the control of convulsions was a very important thing, and a mortality rate up to 83 per cent was dropping very sharply with introduction of proper anesthesia. I think we would regard treatment this way. We would state that the first thing to do with a child with tetanus would be to get in a large dose of antitoxin to neutralize any further toxin that might be developed and prevent further damage to nerves and muscles, but it is of importance here that you cannot administer large doses of antitoxin in a way to invoke a fatal convulsion. When a child has a severe tetanic convulsion, not only obvious muscles are affected but also the larynx is in spasm, and asphyxiation might occur. The first thing to do is to thoroughly sedate the child and then give intravenous and intramuscular injections without danger of stimulating convulsions. Give immediate anesthesia with rectal avertin and adopt 80 mg./kilogram as the initial dose, expecting almost always to have to add another 20, 30, or 40 mg./kilogram in an hour or two to get the proper degree of sedation. It usually takes 100 mg./kilogram to accomplish that with a child with tetanus. Then go ahead with injection of at least 50,000 units intramuscularly and 50,000 units intravenously. Perhaps just one early administration of antitoxin is enough. Then try to keep the child safely in sedation, so that convulsions will not tend to develop. Here you run into difficulty because you may give too little Avertin or not give it often enough and allow the child to come out so completely that a severe convulsion develops. In one instance such a convulsion seemed to have caused death. On the other hand, if you give it in too large quantity and too often, you run a great risk: the blood pressure falls; pulmonary edema may develop; the cough reflex is abolished; if vomiting occurs, aspiration is easy. Constant observation and expert judgment are needed. Special nurses for twenty-four-hour duty are required. Because it seems that dangerous doses of Avertin will be required in order to prevent too-severe convulsions, you consider adding some other substance similar to the Avertin to cut down its dosage. Try to work out a maintenance dose of phenobarbital as an additional sedative, so that you can give less Avertin. After the first eight to ten to twelve hours one begins to think about that. As to the original cause of tetanus, if there is a puncture wound or an area of infection, deal with it surgically while the patient is under anesthesia. Occasionally excision of such an area of infection is resorted to. If it is an old lesion, a scar or a scratch, and no infection is present, we have felt that no excision is needed. It is necessary then to support these children by artificial methods of fluid and food administration. Fluid is more important than food. For the most part these children are in good nutrition and can stand semistarvation if they do not become dehydrated or have severe changes in metabolism. Ordinary salt solution and glucose solution are indicated early, and the intravenous route by

interrupted method is preferred. Fluid given at deep sedation will cause less discomfort. Gradually add to simple fluids those more complete in coverage of food—one can add Amigen, plasma, albumin, and whole blood when there is a real problem of maintaining nutrition. We feel that with gavage, regurgitation and aspiration are facilitated, so we prefer parenteral feeding. Suppose that despite all these measures, treatment still seems not effective. Suppose convulsions do occur or circulatory failure and pulmonary edema develop, or that there has been aspiration with the probability that the patient will develop pneumonia. Is there anything further to do? On two occasions we were forced to consider tracheotomy, and results were miraculous. In the first child it was discovered that obstruction to one main bronchus had occurred and aeration of the other was not too good, and during a convulsion the child had bitten his tongue and aspirated a considerable amount of blood. We wondered if actually we could do a tracheotomy. As it turned out, we had no trouble at all, and a large blood clot was removed. The child then did beautifully and recovered without difficulty. In this child much the same thing developed following epistaxis. In this instance tracheotomy was carried out sooner. It seems it should be done more often and sooner for prevention of laryngospasm. It keeps the respiratory passages free. Can the respirator really be used after a tracheotomy? This can and has been done during a polio epidemic in Minneapolis.

DR. JOSEPH OGURA.—In this patient the problem consisted of pooling of blood from the epistaxis with mucus in the hypopharynx, and with the difficulty in swallowing due to spasm of the pharyngeal muscles and the dropping back of the tongue, laryngospasm, and poor cough reflex and atelectasis occurred. The problem then was similar to those in bulbar polio where, because of laryngeal anesthesia and degeneration of the cells in the nucleus ambiguous, there was likewise aspiration of secretions into the trachea. A tracheotomy was, therefore, necessary in this patient, not only for airway but for aspiration of secretions from the tracheobronchial tree.

What are the methods of therapy other than tracheotomy?

(1) Nasopharyngeal tube by Pearson. Obviously this method will not take care of the laryngospasm that is present.

(2) Endotracheal tube would be of little value inasmuch as it must remain in the larynx much too long with subsequent laryngeal edema.

(3) Intubation. Secretions will be aspirated through the tube.

While preoperative bronchoscopy would be desirable prior to tracheotomy, it was not done because (1) it would stimulate the patient unduly, which we were trying to avoid; (2) there would be difficulty in getting the head in the proper position because of opisthotonos.

Types of Tracheotomy.—It has been said that a high tracheotomy would be more advisable if it became necessary to place the child in a respirator. By definition, a high tracheotomy is an opening above the thyroid isthmus, a low tracheotomy beneath that. A high tracheotomy usually involves going through tracheal rings No. 1 and No. 2. This is not desirable for several reasons: (1)

the tracheal ring would ride on the cricoid. The cricoid is a completely circular cartilage which can be easily damaged when the perichondrium is involved by inflammation. A perichondritis would result. If the inflammation extends forward, a laryngeal stenosis would result. The conus elasticus beneath the mucosa, when involved with inflammation, will result in a cicatricial stenosis. If rings No. 2 and No. 3 are entered, usually this difficulty is not encountered. It is preferable to enter rings No. 3 and No. 4 or lower.

In the Minneapolis bulbar polio epidemic when tracheotomy was done and it was necessary to place the child in a respirator, a high tracheotomy was not done. In their series of bulbar polio cases, in fifteen out of seventy-five tracheotomies thick gray secretions were sucked up into the tracheotomy wounds. In this case, bloody mucus was obtained on opening the trachea. Dr. Holt in Minneapolis devised a method by which a tracheotomized patient could be placed in a respirator. The ring of the respirator into which the head and neck protrude was recessed 3 to 4 inches inward. A funnel rubber sleeve was fitted on this recessed ring and fitted low on the neck. This recessed rubber sleeve low on the neck was held inward into the respirator by a curved metal bar which was attached to the respirator. An additional device was evolved by which there is a three-way inlet which fits onto the tracheotomy tube: an oxygen inlet with a one-way trap valve and an outlet valve; the third outlet was kept closed and used for suctioning. By this method oxygen would be in the closed system and can be humidified to the proper percentage and temperature. Dr. Elam of our Department of Thoracic Physiology has kindly let me show you this apparatus which, he believes, is superior to the apparatus which was used in Minneapolis. It consists of the double rubber sleeve which fits much more snugly on the patient and is held inward by a metal bar which protrudes over the chest of the patient. I would like to point out at this time one important study published in *Pediatrics*, June, 1948, by Goule and Elam. They made oximetric studies using a photoelectric cell to the ear lobe in tracheotomized patients and demonstrated that with the respirator in use, intermittent use of suction through the tracheotomy may reduce the oxygen saturation from a normal of 95 per cent or higher down to an hypoxic state. While suction in bulbar polio or in any tracheotomized patient who needs a respirator is necessary, it should be used cautiously and judiciously.

DR. HARTMANN.—Would you try to make the opening in the second and third rings?

DR. OGURA.—Yes.

Case 5. Growth Failure Associated With Renal Insufficiency

DR. NORMAN HANKIN.—R. K., was 2½ years of age. This child's first admission to St. Louis County Hospital was on Nov. 1, 1946, at the age of 9½ months. Chief complaints then were cough for ten days, drowsiness and dyspnea for the past seven days, and anorexia for the past twenty-four hours.

The past history revealed that he was born prematurely at home in Pacific, Mo., and was cared for at a Washington, Mo., hospital for one month. At the age of 2 months he developed pneumonia and returned to the Washington Hospital where he remained for a month. He seemed to do well, however, until this present admission. The mother was found to have pulmonary tuberculosis when the baby was 4 months of age and was sent to a sanatorium.

Pertinent physical findings in November, 1946, were a greatly retarded, pale, dehydrated infant who was in moderate acidosis and running fever of 102.4° F. At that time a mass could be palpated in the right lower quadrant. Laboratory findings were as follows: carbon dioxide, 26 volumes per cent (11.8 meq. per liter); nonprotein nitrogen, 68 mg. per cent; white blood cells, 14,000; stab cells, 3; segmented, 9, lymphocytes, 86; monocytes 2.

He was treated for his acidosis, placed on chemotherapy and penicillin because of a coincident otitis media (right ear). The persistence of symptoms and presence of the abdominal mass led to I.V. pyelograms which were unsuccessful on two occasions. On Dec. 18, 1946, a cystoscopy was done, and some congenital urethral valves were removed. Because of a persistent finding of pyocyaneus in urine cultures first noted on Jan. 17, 1947, streptomycin was started.

Retrograde pyelography on Feb. 14, 1947, revealed hydronephrosis on the right with bilateral upper ureteral stricture.

On Feb. 24, 1947, the right kidney was explored and found to be enlarged, hard, and nodular with numerous small cysts visible on the surface. The pelvis was dilated tremendously. There was also a stenosis of the ureter about one-half inch distal to the pelvis. This stenotic portion was excised and the lower portion of the ureter anastomosed to the pelvis. A nephrostomy was then done.

The patient had a satisfactory postoperative course, and on March 3, 1947, the left kidney was explored. It was found to be atrophic and nodular, and numerous small cysts were noted on its surface. There was an atresia of the proximal portion of the left ureter. A left nephrectomy was done.

The patient ran a persistent fever, elevated nonprotein nitrogen and low carbon dioxide but was finally discharged after five and one-half months on May 23, 1947. He was placed on 15 c.c. molar sodium lactate three times a day by mouth and was to be followed in the out-patient department.

Since then, this patient has had six hospital admissions for treatment of upper respiratory infections complicated by moderately severe acidosis, anemia, azotemia, and hyperphosphatemia. Between Jan. 24, 1948, and March, 1948, he developed multiple fractures of the right arm, left femur, and left tibia. Each of these admissions has required rather energetic treatment, and retardation of growth and development has been noted in each instance. He has always been discharged on oral molar lactate, calcium, and vitamin D.

This present admission was on July 7, 1948, after an interval of three months with a history of having refused solid foods for the past three to four weeks together with some vomiting. For the past three to four days he has had a rhinitis, nonproductive cough, rapid breathing, skin eruption, and fever.

Physical examination revealed a poorly nourished, dehydrated, greatly retarded, pale infant with acidotic type of respirations. The skin had some small papules (3 to 5 mm. in diameter) scattered over the entire body, especially over the forehead. There was frontal bossing, and the veins of the forehead were prominent and distended. The gingiva of both jaws were greatly hypertrophied. There was a bilateral otitis media present. The spleen was palpable about one fingerbreadth below the left costal margin. He was unable to sit up or talk. There was also some questionable clubbing of the fingers and toes.

The initial carbon dioxide was 25 volumes per cent (11.3 meq. per liter), and the nonprotein nitrogen was 156 mg. per cent. He was treated for acidosis and dehydration with 1/6 molar lactate, and also placed on antibiotics. At the present time he is relatively afebrile and is being maintained on oral molar lactate, calcium lactate, and aluminum hydroxide. He has also been given two transfusions.

Laboratory Data on Last Admission

July 22, 1948	WBC, 8,800
	RBC, 1,510,000
	Hemoglobin less than 7.5 Gm.
	N.P.N., 156 mg. per cent
	CO_2, 25 vol. per cent (11.3 meq. per liter)
	Serum calcium, 7.6 mg. per cent
	Serum phosphorous, 12.0 mg. per cent
July 23, 1948	CO_2 52 vol. per cent (23.1 meq. per liter)
July 24, 1948	N.P.N., 84 mg. per cent
	Creatinine, 4.1 mg. per cent
July 26, 1948	Serum cholesterol, 227 mg. per cent
July 27, 1948	WBC, 9,850
	RBC, 2,980,000
	Eosinophiles 1, segmented 24, lymphocytes 68, monocytes 7
	Hemoglobin, 8.5 Gm.
July 28, 1948	Alkaline phosphatase, 18.8 units
	Phosphorus, 6.5 mg. per cent
	Serum calcium, 9.4 mg. per cent
	Total proteins, 6.38 Gm. per cent

X-ray Studies.—(1) Retrograde pyelogram, April 18, 1947 (Fig. 5). The opaque catheter on the right extends to the ureteropelvic juncture. There is a marked dilatation of the pelvis of the right kidney with a constriction at the ureteropelvic juncture. The condition is due to a marked hydronephrosis of the right kidney.

Showing nephrostomy tube in place, March 14, 1947 (Fig. 6). Examination of the right kidney after injection of opaque solution reveals some dilatation of the superior infundibulum, but the pelvis of the kidney is much smaller, and the minor calices are much smaller than at previous examination.

Skull film, Dec. 12, 1947 (Fig. 7). Examination of the skull reveals a pronounced miliary mottling involving all of the bones. There is definite thickening of the cranial bones, especially in the frontal and posterior parietal regions and to some extent in the occipital region.

Left leg, Feb. 9, 1948 (Fig. 8). There is a transverse fracture of the left tibia with no displacement of the fragments.

Showing calcification of soft tissues, Dec. 6, 1947 (Fig. 9). Both lower extremities are shown.

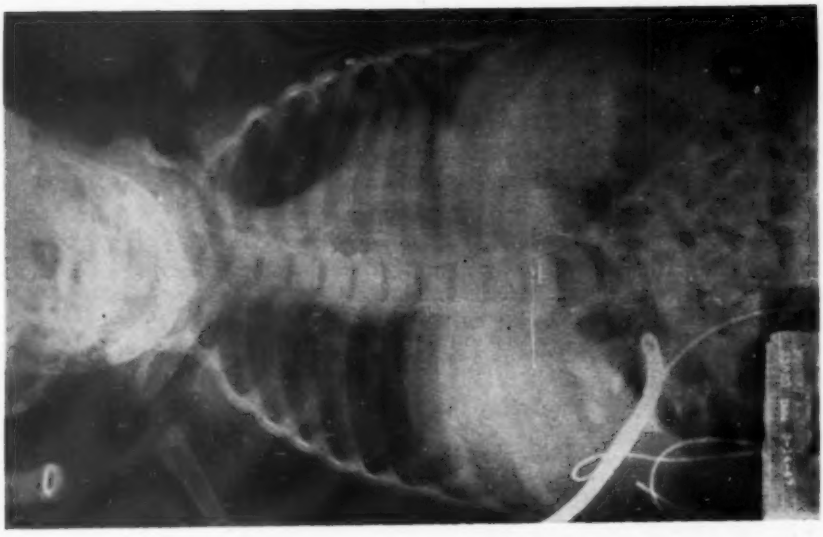

Fig. 6.

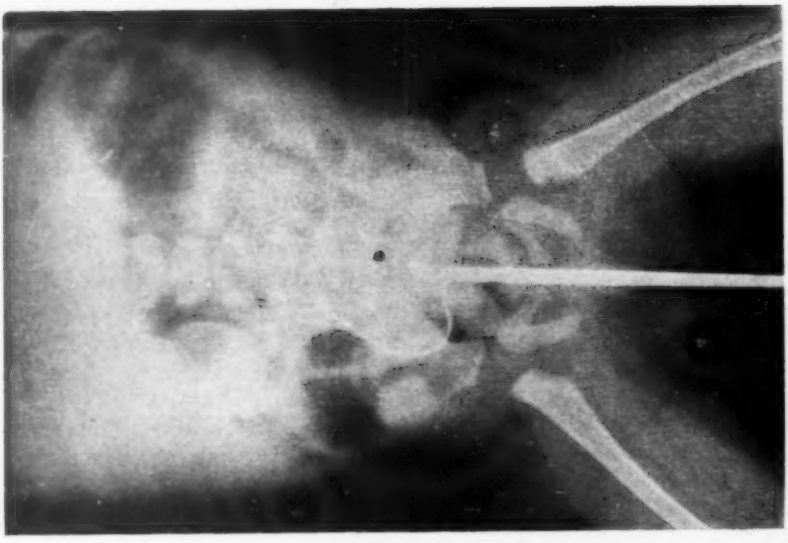

Fig. 5.

Fig. 7.

Fig. 8.

Fig. 9.

DR. LEO GOWEN.—We are presenting this child as a case of primary renal insufficiency with secondary compensatory hyperparathyroidism. The renal insufficiency is due to polycystic kidneys; an atrophic, polycystic, functionless left kidney has been removed, while on the right side the ureter was found stenotic and dilated proximally, with resultant hydronephrosis and stasis infection. Surgery has relieved the obstruction in the right ureter, and antibiotics and improved urinary drainage have controlled the infection. That portion of the remaining kidney which functions does so poorly as manifested by the high degree of nonprotein nitrogen retention and hyperphosphatemia. A poor prognosis is to be seen in the very low and still decreasing values of the urea clearance tests and the increasing degrees of azotemia and phosphatemia and the persistent acidosis. The latter seems due chiefly to failure of reabsorption of fixed base (chiefly sodium) because of damaged tubules, but is also contributed to by failure of excretion of fixed anion, particularly phosphate, which results in hyperphosphatemia. There is to be noted some reciprocal fall of serum calcium, but without tetany, probably because of the relatively increased calcium ionization brought about by the acidosis (increased H^+ ion concentration of the blood). Hyperparathyroidism, secondary it is usually thought to the hypocalcemia, probably accounts for the depletion of the calcium stores of the body. The soft tissue storehouses of calcium are thought to be called upon first until depleted, and then the hormone turns to the base of the skeletal structures. In bone there is considerable sodium which first may be used to neutralize ordinary acids of metabolism. The calcium of the matrix of bones is then drawn into the blood serum. As a result there is a generalized decalcification of the skeleton similar to atrophic rickets. If epiphyseal growth occurs, as did in this child, bending and distortion of the long bones may occur, giving rise to what is termed by some "florid rickets." Finally a fuzzy appearance of the bone with cystic change may be noted, along with calcification in the soft tissues, which is usually referred to as "woolly bone changes," osteitis fibrosis cystica, or osteoporosis.

Renal "dwarfism" has been noted in five different conditions of renal insufficiency: (1) chronic glomerulonephritis, (2) congenital polycystic kidneys, (3) pyelonephritis, (4) renal hypoplasia, (5) hydronephrosis.

Various names have been used to designate the status of this child's syndrome; viz.

(a) Renal rickets, which is not adequate, for skeletal changes are not those of rickets but of an osteoporosis.

(b) Renal dwarfism, which does not describe the picture, for "dwarfism" implies only smallness of size, whereas deformities are also present.

(c) Renal infantilism would only be of some value for those patients who were in infancy.

(d) Osteitis fibrosa cystica which term suggests an inflammatory etiology, whereas the term renal hyperparathyroidism with osteoporosis fibrosa cystica, indicates not only the bone pathology but also the etiologic systems involved, and implies the sequence of pathologic physiology.

Important in caring for this child have been: (1) combating infection and avoiding reinfection; (2) frequent transfusions because of hypoplastic bone marrow; (3) furnishing large amounts of water to counteract effects of polyuria; (4) replacing sodium, which is constantly being lost via urine, by giving sodium lactate between meals; (5) giving calcium orally (after meals with the hope that it may be absorbed better in an acid pH of the small intestine); (6) giving adequate vitamin D and orange juice to favor the absorption of calcium; (7) avoiding high fat in the diet; (8) providing high alkaline ash foods; (9) using aluminum hydroxide in addition to calcium to lessen the absorption of phosphate from the intestine; (10) replacing chloride ion when lost by vomiting; (11) administering sufficient lactate to control acidosis.

Because of the findings in this case of polycystic kidneys associated with infection and chronic renal insufficiency and acidosis, hyperphosphatemia, hypocalcemia, and increased phosphatase activity, with generalized osteoporosis and deformities without hypertension, we feel that the pateint conforms to the diagnosis of renal hyperparathyroidism with osteoporosis fibrosis cystica.

DR. ALEXIS HARTMANN.—This is an amazing case, a typical example of growth failure associated with renal insufficiency and very profound disturbance of bone growth. When Dr. Gowen enumerated the different renal causes for failure of development, I thought of a sixth one which we have seen—nephrocalcinosis. At least four of the causes are here: (1) polycystic kidney, (2) hypoplasia, (3) persistent infection, and (4) bladder neck obstruction with hydronephrosis. We are pretty sure that there is no glomerulonephritis, but not so sure that nephrocalcinosis is not also present.

One question is of interest and fundamental in arriving at a conclusion. First attempts made to explain the decalcification of bones were along lines of altered acid-base balance, and it was first assumed that chronic acidosis developed and led to abnormal excretion of cations from the body, largely sodium and potassium, but later calcium and magnesium. That led to rickets or bony changes called rickets and which resembled changes of hyperparathyroidism. One interesting case in particular was studied by Boyd and Stearns. They reported a case of persistent rickets with chronic acidosis as the only apparent cause, where alkali administration alone was successful in controlling the rachitic process. Recently, however, it has been demonstrated that ordinary vitamin D rickets can be treated quite successfully without vitamin D but by dietary measures which provide intestinal acidity with alkaline ash. Only two buffer substances are effective, citric acid and sodium citrate or tartaric acid and sodium tartrate. Lactic acid and sodium lactate are not very successful.

Do you have any evidence that after prolonged alkalinization any improvement in the skeletal process took place? This child has received 200 c.c. molar sodium lactate daily or almost 30 c.c. kilogram. Dr. Gowen, when you tested the pH of urines with nitrazine paper, you very often found it to be very alkaline, and fresh urines approached a pH of 8. This is very interesting

and important to verify, because our concept would be that any child with only one kidney, and that so badly involved, would not have the ability to concentrate sodium bicarbonate any more than he would have the ability to concentrate anything else. It would be well to determine the carbon—dioxide content of freshly passed urine to see what there is in the way of sodium bicarbonate in the urine. Is there any evidence that alkali therapy has changed the skeletal picture in this child?

DR. GOWEN.—I do not know whether I can answer that, Dr. Hartmann.

DR. HARTMANN.—Well, that would take considerable study. From your plates, such therapy would not seem to have changed it. I think these skeletal changes are principally due to the hyperparathyroidism.

DR. PETER HEINBECKER.—I wish to suggest briefly a possible endocrine basis for the dwarfism exhibited by this child. Normally there are three types of cells in the glandular division of the hypophysis, existing in a balanced relationship. Two of these, the eosinophiles and the basophiles, are secretory. The eosinophile cells are the source of the growth hormone. It is accepted that the hypophysis, as the master gland, is trophic or inhibitory to the other endocrine glands. What is not realized so generally is that it is, in itself, subject to modification by these same endocrine glands. Six months after adrenalectomy with maintenance on doca (desoxycorticosterone acetate) pellets there has resulted a marked disappearance of eosinophiles. The growth-stimulating potential of such an hypophysis would be reduced greatly. In support of this is the evidence that pups with only enough adrenal tissue left to support life show a marked retardation of growth. Likewise it has been shown in our laboratory that the hypophysis of a dog with one kidney removed and the other wrapped in silk to produce hypertension, shows a great increase in eosinophile cells and a decrease in chromophobes. The width of the adrenal cortex of such a dog is widened. Similar effects are produced during the period of hypertension when one kidney is left intact and the other wrapped in silk. Presumably a lessening of blood flow to the normal renal tubular tissue is responsible for the release of the hormone (renin?) when kidneys are so treated. The hormone released from the kidney effects an increase in the number and the secretory capacity of hypophyseal eosinophile cells.

In this patient there is evidence that the renal tubules are functionally depressed, probably greatly reduced in number. As a consequence it is reasonable to suspect that they would secrete an inadequate amount of the hormone believed essential for the maturation of hypophyseal eosinophile cells. The diminution in number and effectiveness of such cells would be expected to interfere with normal growth. It would lessen the efficacy of the adrenal cortex. Many of the chemical disturbances exhibited by this child suggest adrenal cortical deficiency. The failure of the growth hormone would decrease the growth of the other hypophyseal cells, including the basophiles. These cells, in other studies, have been found to be inhibitory to the parathyroid glands. Consequently, their decrease would permit overaction of the parathyroid glands.

In summary, then, on the basis of experimental evidence and on evidence presented here this morning, it is suggested that a marked defect, primary in the renal tubules, could be expected in the young to cause changes in the hypophysis, in the adrenal glands, and in the parathyroid glands, of a nature and direction to produce the clinical picture exhibited by this child.

DR. JOSEPH JAUDON.—If pituitary dwarfism is based on overaction of the parathyroid and underaction of the adrenals with contrarenal enlargement of that kidney after being wrapped in silk, do you have other evidence of increased growth of other tissues other than the adrenals and kidney?

DR. HEINBECKER.—Not ordinarily, except where you get acromegaly.

Psychologic Aspects of Pediatrics

BREAST FEEDING

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ALTHOUGH it is generally agreed by obstetricians and pediatricians that breast milk is the preferred food for infants, the incidence of breast feeding is declining.[1] Moreover, the duration is becoming shorter. In England and Wales 80 per cent of the babies born in hospitals and 95 per cent of the babies born at home are entirely breast fed. Whether the infants are born in the hospital or at home, by the end of three months only 50 per cent and at the end of six months only 40 per cent continue to be breast fed.[1, 2] Statistics on breast feeding in this country would show a much lower incidence.

The reasons for the decline in breast feeding are numerous. Perhaps most important is the ease and success of artificial feeding. Many women have an aversion to breast feeding, looking upon it as an activity suited only for lower animal forms. There is a false impression that breast feeding is confining. Hospital delivery with the premature use of artificial feeding before the breast milk comes in and the early resort to complementary feeding contribute to the failure of maternal nursing. In many hospitals breast feeding is discouraged as it interferes with the "routine" of the nursery.

In the early days of artificial feeding, efforts were directed toward devising a milk mixture which would duplicate in chemical composition the mother's milk. With this idea in mind, cow's milk was diluted to reduce the concentration of protein, and sugar was added to raise the carbohydrate content. By using "top milk" for dilution the concentration of fat was maintained at the level of mother's milk. It was quickly discovered that the differences between the two milks were much more diverse and subtle than had been originally suspected. But, despite this, babies thrived on the artificial mixtures and, with the years, the effort to simulate breast milk has been abandoned. It has gradually come to be accepted by many that, great though the differences between human and cow's milk may be—and the number of differences being discovered is growing—cow's milk is just as good as human milk as a food for infants.[3] However, the criteria of adequate feeding are still not well established and the significance of the metabolic differences between the infants receiving the two milks have yet to be determined.

More recently, interest has shifted to the psychologic aspects of breast feeding and there are some who consider that the emotional value of this procedure represents the principal, if not the sole advantage of maternal nursing. With this in mind they advocate duplicating as nearly as possible in artificial feeding the method of holding the baby, cuddling, etc., as is done during breast

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feeding. These maneuvers are analagous to the early attempts at modifying cow's milk to make its composition similar to that of human milk and, again, assume a knowledge of the numerous factors implied in the breast-feeding situation which is not justified.

DIFFERENCES BETWEEN HUMAN AND COW'S MILK

It is not our intention to present a detailed review of the differences between human and cow's milk. Excellent studies along this line have been recently published by Macy and associates.[4] We wish to mention here only certain differences, recently discovered, which illustrate further the complex ways in which the two milks differ.

Protein.—The total protein content as well as the proportion of casein to lactalbumin varies in different milks. Cow's milk contains approximately 2.8 per cent casein and 0.5 per cent lactalbumin; human milk 0.5 per cent casein and 1.0 per cent lactalbumin. Williamson[5] has shown that, if cow's milk is diluted to make the total protein content equal to that of human milk, noteworthy differences between the character of the proteins remain. Human milk contains three times as much cystine and a larger amount of tryptophan than does the diluted cow's milk. On the other hand, the diluted cow's milk proteins contribute over one and one-half times as much methionine and about 20 per cent more histidine, threonine, and valine than the human milk proteins.

Recent studies indicate that the behavior of casein of human and cow's milk differs.[6] By means of electrophoretic analysis it has been possible to separate casein into two or possibly three fractions of different chemical composition. The relative amounts of these fractions differ in human and cow's milk. Moreover, in vitro digestion experiments using pepsin, trypsin, and human adult gastric juice, show a considerable difference in the digestibility of casein, the cow's milk casein being more readily and completely hydrolyzed than that of human milk.

Fat.—Both human and cow's milk contain about 3.5 per cent of fat. Hilditch and Mara[7] have recently shown that the composition of human milk fat differs from that of butter fat particularly in the fatty acid content. Human milk fat contains about 7 per cent linoleic acid, whereas there is little or none in cow's milk. This is one of the unsaturated fatty acids which is essential for the nutrition of rats.[8] It has also been shown that there is a relationship between the metabolism of fats and lactose, the utilization of the sugars apparently being dependent on the presence in the diet of certain fatty acids.[9]

PHYSIOLOGIC DIFFERENCES BETWEEN BREAST- AND ARTIFICIALLY-FED INFANTS

Nitrogen Retention.—Catherwood and Stearns[10] have shown that the proportion of ingested nitrogen which is retained by infants receiving human and cow's milk is about the same, but since cow's milk contains about twice as much protein, infants receiving cow's milk retain a correspondingly larger amount of nitrogen. They, therefore, have a relatively larger store of tissue protein than breast-fed babies, some of it occurring as muscle. This is of doubtful

value. Jeans[11] has shown that, when cow's milk is diluted so that nitrogen retention is reduced to equal that of a breast-fed infant, tissue turgor is poorer and motor development is impaired. Undoubtedly unknown factors in the nature of the proteins of cow's and human milk are involved. The difference in protein retention may be related to the different rates of gain in weight of infants fed breast and cow's milk. Faber and Sutton[12] have shown that, during the first three months of life, breast-fed infants show a significantly better mean weight gain than bottle-fed infants. Later, artificially-fed infants gain more rapidly and this superiority becomes progressively greater up to the time of weaning.

Carbohydrate Metabolism.—Lactose is the sole carbohydrate of milk; human milk contains about 7 per cent and cow's milk 4.5 to 5 per cent. Aside from its value as an energy yielding constituent, it may, by its effect on intestinal microflora, affect the synthesis of various nutrients.[13] Lactose promotes the absorption of calcium and phosphorus, presumably because of its influence on the acidity of the gut contents. It is generally assumed that the lactose of human and cow's milk behaves in the same manner, but recent observations of Natelson, Kramer, and Sherman[14] indicate that raw mother's milk feedings cause higher blood sugar rises than do similar amounts of lactose in evaporated milk or in raw cow's milk.

Calcium and Phosphorus Retention.—Cow's milk contains, on the average, about four times as much calcium and about six times as much phosphorus as human milk. About two-thirds of the phosphorus in cow's milk is excreted by the infant in the urine. Though the percentage of ingested calcium and phosphorus retained by infants receiving cow's milk is smaller than that retained by infants on mother's milk, the actual amount stored is greater. As a result the percentage composition of infants receiving cow's milk is higher in calcium and phosphorus than that of breast-fed infants. Stearns[15] has shown that during early infancy, when a baby is fed wholly on the breast, the concentration of calcium in the skeleton decreases rapidly and probably does not reach the birth value before the first birthday. This does not mean that the infant is in negative calcium balance but probably indicates that the newborn infant has stored calcium in the skeleton. When, on the other hand, cow's milk is given, a smaller decrease of calcium concentration in the skeleton occurs and several weeks after birth the concentration starts to rise. The significance of these differences is not clear. While it is true that the linear growth of babies fed a standardized cow's milk formula is related to the amount of calcium retained, the breast-fed baby shows excellent linear growth despite the much lower calcium retention and grows at a definitely greater rate than the artificially-fed baby with the same calcium retention.[16] There is no evidence to show that the baby who stores more calcium has any nutritional advantage.

It is of interest that, despite the greater retention of calcium and phosphorus by infants receiving cow's milk, rickets is likely to be more severe among them and tetany much more common. In neither human nor cow's milk have important quantities of vitamin D been found. Perhaps the various relationships of the components of human milk are such that calcium and phosphorus

are more efficiently utilized from this food than from cow's milk. Harris and Bunker[17] have suggested that there may be a specific superiority of the vitamin D content on mineral interrelationships in human milk.

The tetanogenic property of cow's milk has been known for many years and has been attributed to its high phosphorus content. Finkelstein[18] was able to allay the symptoms of tetany by substituting human milk for cow's milk in the diet of affected infants. Bakwin[19] has shown that the feeding of phosphorus to newborn infants leads regularly to a reduction in the serum calcium and he suggests that the early feeding of cow's milk is a factor in the pathogenesis of tetany of the newborn infant.

Vitamin C Retention.—Raw cow's milk under market conditions contains between 1 and 2 mg. of ascorbic acid per 100 c.c. and pasteurized milk about one-half this amount. This compares with from 3 to 4.5 mg. per 100 c.c. in human milk. It appears that breast-fed infants utilize ascorbic acid better than artificially-fed infants. Snelling[20] found higher ascorbic acid levels in breast-fed infants than in artificially-fed infants receiving equivalent amounts of vitamin C in orange juice. The possible reasons for this are that breast feeding enhances the absorption of vitamin C or that the continuous administration throughout the whole day allows for more complete absorption. Bakwin[21] has also reported that the artificially-fed infant requires from 75 to 100 mg. of vitamin C daily to get the same blood levels as the breast-fed infant. Dann[22] has shown that premature infants receiving boiled human milk retain a larger part of a "saturation" dose of ascorbic acid in their tissues than do infants given cow's milk. She offers the hypothesis that the increased daily requirement of vitamin C is related to the high level of protein from cow's milk. This explanation is in accord with the work of Levine and his co-workers[23] who have shown that ascorbic acid is concerned with the intermediary metabolism of aromatic amino acids.

Resistance to Infection.—There is a great deal of evidence to show that breast-fed babies are less prone to gastrointestinal disturbances and respiratory infections than artificially-fed infants. The frequently quoted work of Grulee and his associates[24] clearly indicates the superiority of breast feeding in this respect. In a study of 26,061 babies under the care of the Infant Welfare Society of Chicago, the incidence of infections of all types in the breast-fed group was 37.4 per cent as compared to 63.6 per cent in the artificially-fed group. Of the breast-fed group, 28 per cent suffered from a respiratory infection of some type as compared to 37 per cent of the artificially-fed; 5.2 per cent of the breast-fed group had various gastrointestinal disorders as compared to 16 per cent of the formula-fed infants. Of 218 deaths occurring in this group 15 or 6.7 per cent were in the breast-fed infants and 144 or 66.1 per cent in the artificially-fed group. Breast feeding apparently gave a much greater immunity to infection than artificial feeding. These findings have been confirmed by other investigators. Ebbs and Mulligan[25] examined the records of 1,500 consecutive admissions of babies under 12 months of age admitted to the Hospital for Sick Children in Toronto for various infections. Of this number only 15.1 per cent were wholly breast fed, 29.1 per cent had been breast fed for

at least six weeks, and 55.7 per cent were artificially fed from birth. The incidence of breast feeding among these 1,500 infants with infections was less than half the incidence of breast feeding in the well-baby clinics in the city. Smellie[26] reported 375 infants below the age of 9 months with diarrhea. Only 154 or 41 per cent had been breast fed for a month or more. The mortality rate in this group was 25.9 per cent, which contrasts with a mortality rate of 76.6 per cent in those who never had been breast fed. Robinson[27] studied 240 infants for a period of twenty months, noting the gastrointestinal disturbances and rashes following different feedings. The breast-fed infants had the lowest incidence of diarrhea and rash. Stevenson[3] analyzed the records for the first year of life of 263 infants, of whom 95 were breast fed for three months or longer. He found a higher incidence of respiratory infections among the artificially-fed infants during the second half year of life (1.43 respiratory infections per artificially-fed infant and 0.95 respiratory infections per breast-fed infant). There was no significant difference in the amount of diarrhea and miscellaneous infections between breast- and properly artificially-fed babies.

Diarrhea of the Newborn Infant.—According to Rice and his associates[28] the breast-fed is about as susceptible as the artificially-fed infant. However, they mention that it is routine practice in hospitals to give breast-fed infants some form of additional food or fluid during the first week. Therefore, the rubber nipple as a source of infection cannot be ruled out. Cron and co-workers[29] describe an epidemic of diarrhea in a nursery. Of this group eighteen of twenty-five babies being formula fed died. Six babies who received breast milk plus formula and eight more who obtained breast milk after having been on formula for three or four days either did not contract the disease or, if they did, survived their illness. Ormiston[30] describes an outbreak in which six out of fifty-one sick infants entirely breast fed died, contrasted with ten out of thirty given cow's milk with or without breast milk. Sakula[31] reports eighteen newborn infants in a nursery who contracted gastroenteritis, of whom fifteen died. The outbreak was confined to bottle-fed infants.

It is true that the technique of breast feeding as compared with artificial feeding allows fewer channels for infection of the infant. However, it seems that breast feeding gives the infant an added measure of protection against both respiratory and gastrointestinal infections. The mechanism for this is not clear. The antibodies of human serum are contained mainly in the gamma globulin fraction. Longsworth and his associates[32] have shown that both the absolute and relative concentrations of fetal gamma globulin are higher than either the normal or maternal value. Placental transmission of antibodies and not breast milk is responsible for this. Investigations have shown that colostrum is incapable of increasing the level of diphtheria antitoxin in the blood of infants.[33] However, there has been little work done on the possible transmission of virus antibodies through colostrum or milk. In this connection it is of interest to note that Berry and Slavin[34] have shown that mice could be passively immunized through the mammary route against infection with herpes virus. This naturally acquired immunity declined rapidly when suckling was interrupted. Whatever the mechanism may be, it is obvious that breast feeding.

even though it be for a short period, offers the infant some degree of protection against gastrointestinal and respiratory infections.

Eczema.—Grulee and Sanford[35] have shown that the general incidence of infantile eczema is lowest in breast-fed infants. In the partially breast-fed infants, eczema was twice as frequent as in the breast-fed, and in the artificially-fed, seven times as great. There is as yet no conclusive evidence for demonstrating a causal relationship between sensitization of the newborn infant and the passage of proteins through the breast milk.[36]

PSYCHOLOGIC ASPECTS OF INFANT FEEDING

The interrelationships which are set up between mother and child during the early days and weeks of life set a pattern which is important for the later development of the child. The mother who nurses her baby establishes, at an early date, an intimacy with her child which makes further relationships with him easy and natural. Czerny, a strong advocate of breast feeding, stated that "between the person (who nurses the baby) and the child those relationships develop which are most highly valued when they exist between parent and child. For the child fed by a wetnurse or a nurse, the mother remains a stranger despite the blood relationship, and the less often the infant sees the mother the stronger becomes the estrangement. The mother who does not feed the child herself creates, already in the first year of life, a barrier between herself and the child which is never completely removed." [37]

Breast-feeding provides the mother with a sense of satisfaction and a sense of achievement which is not readily obtained otherwise. In no other way can she so well demonstrate her indispensibility to the child. The mother who nurses her baby has him at her side in the hospital five or six times a day. The rooming-in system, by which the mother is permitted to have the baby in her room, loses much of its value if breast feeding is not established, since the benefit derived from the early nearness of the baby is not continued. These considerations are especially important when the mother has strong interests, business, professional, or social, outside the home.

For the baby, too, breast feeding provides emotional satisfactions which appear to be highly important to him. The newborn infant is endowed with a fairly well-developed set of emotional responses. These responses must be elicited by stimuli applied from without through the senses since the newborn infant, lacking cerebral power and experience, is unable to originate emotionally charged situations. Though all his senses are developed and functioning, vision means little to him since, to a very large degree, the interpretation of visual stimuli requires experience. The same is true of auditory stimuli, although here the sound of a cooing voice seems to be soothing. The other senses, smell, taste, the skin sensations, and muscle balance require no experience and appear to be highly meaningful to the young baby. He is readily quieted by warmth, by patting and stroking, and by being allowed to suck. These satisfactions are provided automatically while feeding at the breast. How vital they are for the welfare of the young baby is seen in those cases where the infant is

deprived of such stimulation, as, for example, when hospitalization becomes necessary. In this situation babies wilt quickly and, if deprived for an extended period, many die.[38]

Infants receiving breast milk more readily regulate their intake than do those on cow's milk. The cautious physician, aware of the danger of intestinal upset during the early weeks of life, will hesitate to give the large amounts of food often required by the infant at this time.

It is not our viewpoint that all babies who are breast fed will grow up to be happy adults or vice versa. We do feel, however, that it is one step, and an important one, in establishing proper interrelationships between mother and child, and in providing suitable outlets for the young baby's budding emotional needs. In addition, under proper circumstances, it supplies a satisfying experience for the mother.

In advising breast-feeding, care must be taken not to stress its importance to such a degree that the mother will feel herself inadequate or blameworthy if it becomes impossible for her to nurse her baby.

SUMMARY

A survey of available data shows that the reaction of infants to human and cow's milk differs in many respects. The differences are reflected in shape of the growth curve, in the amounts of nitrogen, calcium, and phosphorus which are retained, in the plasma vitamin C levels, in the response of the blood sugar to lactose ingestion, in the incidence and severity of vitamin D deficiency disease and eczema, in the incidence of tetany during the newborn period, and in the frequency of respiratory infections. It is not our intention to present these data as evidence of the superiority of human over cow's milk in feeding babies, although the lowered incidence of respiratory infections and severe eczema in the breast-fed infant is a very real, practical consideration. Reasoning from the meager available information, it would appear that breast feeding is superior to artificial feeding from the psychologic viewpoint.

In the last analysis, the choice of one or the other method of feeding stems from a general attitude. The physician who is impressed by the remarkable adaptibility of the human organism will, whether giving advice in the care of a well child or in ministering to the sick, interfere minimally with natural processes. We have erred too often in the past.

This is not meant to minimize in any way the enormous value of artificial feeding for those infants who, for one reason or another, are unable to be fed at the breast. We do feel, however, that artificial feeding should be reserved for the instances where an honest attempt at breast feeding has failed.

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Comments on Current Literature

BRUCELLOSIS

THE August (1948) issue of the *Annals of Internal Medicine* carries an instructive discussion of human brucellosis by Dr. Wesley W. Spink,[1] who points out that the incidence of brucellosis both in domestic animals and in human beings is on the increase. During 1947 more cases were recognized and reported in the country as a whole than in any previous year.

The disease has its reservoir in domestic animals, particularly cattle, hogs, and goats, and three closely related species responsible for human disease, have been identified: *Brucella melitensis, Brucella suis,* and *Brucella abortus. Brucella melitensis* is found primarily in goats, although it has also been shown to infect cattle. A fact of considerable epidemiologic importance was brought to light recently by the findings in Iowa and Minnesota that *Brucella melitensis* is distributed widely in hogs. The hog is the natural reservoir for *Brucella suis.* However, *suis* has been reported in cattle. *Brucella abortus* occurs primarily in cattle with localization in the udder and in the pregnant uterus of heifers. Infection in man seems to be incidental in the natural history of brucellosis, since the disease is primarily one of domestic animals.

There are two principal routes by which infection occurs in human beings the first by consumption of raw milk and milk products from diseased animals, and the second through contact of the human skin with the tissues, secretions, or excretions of animals with brucellosis. In addition to these common modes of transmission, occasional infection has occurred in persons handling cultures of Brucella in the laboratory. The possibility of air-borne infection and the inhalation of viable Brucella cannot be dismissed.

Dr. Spink points out that the tissue responses to this infectious agent are rather characteristic, organs belonging to the reticuloendothelial system, the spleen, liver, bone marrow, and lymph nodes, being invaded consistently by Brucella. A second feature of importance is the intracellular parasitism of parenchymal cells by these microorganisms. Dr. Spink quotes from studies by Meyer[2] which were made on the tissues of a patient within three weeks of a fulminating infection: "This selective intracellular parsitism in mesenchyme cells of various organs is doubtless of greatest significance in the pathogenesis of Brucella infections." Spink and his associates[3] have been interested for some years in the histopathology of tissue reactions in brucellosis, both in experimental animals and in living patients by biopsy techniques. Excellent photomicrographs are included in Spink's article which show the typical granulomatous lesions of various tissues. The outstanding features are proliferation of epithelioid cells with or without giant cells and the presence of lymphocytes, plasma cells, and occasionally eosinophiles.

Of considerable interest is the fact that in three patients in whom repeated cultures of blood showed no growth of organisms, Brucella organisms were cultured from the sternal marrow. Another interesting pathologic feature of the disease is the involvement of the liver. As early as 1939 the statement was made[4] that the most common visceral lesion occurring in brucellosis involves the liver. On the basis of their investigations, Spink and his co-workers are inclined to agree, believing that the hepatic changes should not be considered a complication, but rather a part of the natural history of the disease.

Unusual complications of brucellosis include osseous changes involving the vertebrae, the pelvis, and the long bones. In this connection Spink states that while periarticular distress is not uncommon in brucellosis, the group at Minnesota has not encountered a single case of chronic arthritis resulting from brucellosis. Another complication encountered in their series of cases was subacute bacterial endocarditis. Four cases due to *Brucella abortus* were studied and treated. Three of these patients had fatal illness, but the fourth recovered and remained well for over a year following combined treatment with streptomycin and sulfadiazine.

In a section devoted to immune reactions Spink emphasizes the development of hypersensitivity following invasion of the tissues and states that "although it may not be illogical to subject patients with chronic brucellosis to increasing doses of Brucella antigens in attempts to 'desensitize' their tissues," their own "efforts in the therapy of brucellosis have been toward eradicating viable Brucella from the tissues, thus ridding the body of the source of antigenic material."

Accordingly, the Minnesota group favor the combined use of streptomycin and sulfadiazine in an attempt to eradicate Brucella from the body. These agents act in a synergistic fashion and are not merely additive in their effect. Carefully tabulated clinical results with this combined therapy were verified by experimental studies in embryonated hen's eggs infected with brucellosis.[3] All three species of Brucella were investigated.

The clinical observations cover a period of approximately one year. Seventeen patients with brucellosis were treated with streptomycin and sulfonamides, especially sulfadiazine. In fourteen of these patients *Brucella abortus* was isolated. Nine of the cases were designated as the acute form of the illness, being of less than three months' duration. From eight of the nine, *Brucella abortus* was isolated. In general the results were good, and from study of these nine cases, Spink concludes that eight to ten days of combined treatment are required before patients experience definite improvement with return to normal temperature.

Eight patients, in whom the illness was of three months' duration or more, were classified as chronic cases, and from six of these eight patients *Brucella abortus* was isolated. In this group of chronic cases, results of combined therapy were quite similar to those obtained in the acute cases. Slightly larger amounts of streptomycin were administered to the chronically ill patients. On the basis of experience with these seventeen patients, Spink recommends that the total daily dose of streptomycin should not exceed 2 Gm. However, 0.5 Gm. of streptomycin may be given intramuscularly every six hours for two weeks and at the same time 3 to 4 Gm. of sulfadiazine may be administered orally in an initial dose and then 1 Gm. every four hours for a total of three weeks. Spink emphasizes the desirability of hospitalization under close supervision for all patients undergoing therapy, since toxic complications are possible and may be serious.

In a discussion of prevention, Spink points out that "every effort must be made to eradicate the animal reservoir of the disease." He enumerates some of the difficulties involved in this problem, particularly as species of Brucella are more widely distributed than was realized formerly. Since no dependable methods of immunization against brucellosis are known for man, control measures are of even greater importance. Danger of contact with infected animals must be emphasized, for brucellosis may become a real occupational hazard for farmers, livestock workers, veterinarians, and abattoir workers.

While it is generally accepted that cow's milk must be pasteurized, there seems to be considerable laxity concerning regulations for the pasteurization of

goat's milk. The increasing awareness that brucellosis is a real medical problem must bring about adequate pasteurization of all milk and milk products, goat included. Implications that the nutritive value of goat's milk is altered by the pasteurization process seem completely unfounded.

Spink poses questions regarding mild, inapparent infections in children and adults. Recognized brucellosis is less frequent in children under 12 years of age than in older age groups, and increased resistance of young children to brucellosis seems to be an established fact. Immune studies carried out by the Minnesota group and elsewhere indicate that the tissues of rural children are invaded by Brucella, and that mild infections do occur. Accurate information is not available as to whether one attack or mild infection confers immunity against subsequent attacks. With improved methods of diagnosis and study it seems possible that many more cases in the pediatric age group may be recognized.

RUSSELL J. BLATTNER.

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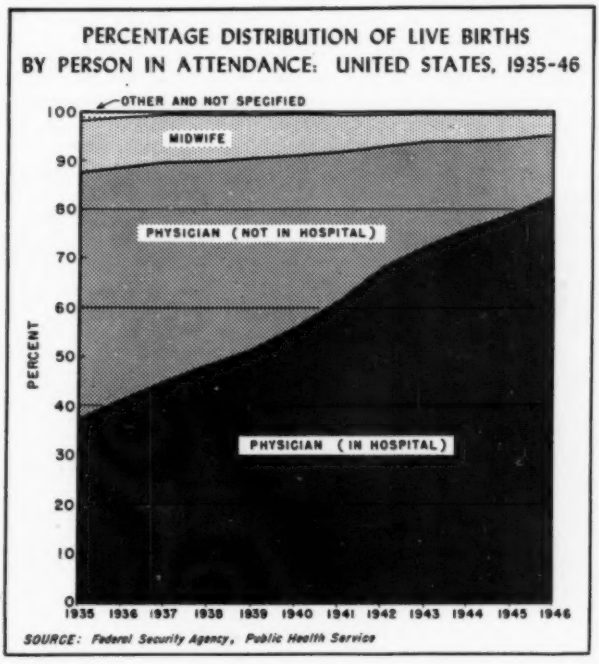
News and Notes

According to statistics recently released by the National Office of Vital Statistics, a new record was set in 1946 for births delivered in hospitals. Of 3,288,672 live births recorded in 1946, 82.4 per cent occurred in hospitals. Connecticut led with 98.9 per cent, with Washington second with 98.2 per cent. The New England and Pacific Coast states were highest as groups, with the southern states the lowest. The marked increase in hospital births that has taken place since 1935, when such data were first compiled, is shown in the following graph prepared by the Federal Security Agency.



The **American Board of Pediatrics** will hold examinations at St. Louis, Mo., on Feb. 18, 19, and 20, 1949, and at Baltimore, Md., on April 22, 23, and 24, 1949.

The following were certified by the **American Board of Pediatrics** at the examination in Seattle, September, 1948:

Dr. Mason H. Abramson, 90 Birch Street, Redwood City, Calif.
Dr. Forrest Hood Adams, University of Minnesota Hosps., Minneapolis 14, Minn.
Dr. Albert T. Aldrich, 153 S. Lasky Drive, Beverly Hills, Calif.
Dr. Wesley Huntington Anderson, 412 First Security Bank Bldg., Ogden, Utah.
Dr. Victor J. Birnberg, 6333 Wilshire Blvd., Los Angeles 36, Calif.
Dr. George Orion Boucher, 529 E. Tenth Street, Long Beach 13, Calif.
Dr. Mathew D. Burnett, Jr., 5101 Fannin Street, Houston, Texas.

Dr. Charles Macfie Campbell, Jr., 911 Chapala Street, Santa Barbara, Calif.
Dr. Michael Joseph Campbell, 7943 Exchange Ave., Chicago, Ill.
Dr. Leroy O. Carlson, 717 Baker Bldg., Walla Walla, Wash.
Dr. R. Wendell Coffelt, 628 North Glenoaks, Burbank, Calif.
Dr. John R. Connell, Children's Hospital, Denver, Colo.
Dr. Lewis T. Corum, 241 Lafayette Arcade Bldg., Tampa 6, Fla.
Dr. James Otis Dowrie, 1205—24th St., Sacramento 16, Calif.
Dr. Josephine Lewis Earlywine, 1159 Wilmette Ave., Wilmette, Ill.
Dr. Frank L. Fletcher, 311 W. Idaho, Boise, Idaho.
Dr. Thomas V. Geppert, The Henry Ford Hospital, Detroit, Mich.
Dr. Grace Baker Goebel, 469 Chapman Drive, Corte Madera, Calif.
Dr. Margaret L. Goetsch, 110 W. Broadway, Glendale, Calif.
Dr. Martha Helen Hale, 3403 Hall, Dallas, Texas.
Dr. Herbert Bryan Hutt, 42 W. Midlothian Blvd., Youngstown 7, Ohio.
Dr. Julius M. Kantor, 306 East 12th St., Kansas City, Mo.
Dr. Frank McCarry, 451 Paulsen Medical and Dental Bldg., Spokane, Wash.
Dr. John Patrick McDermott, 515 Cobb Bldg., Seattle, Wash.
Dr. Donald Hemphill McDonald, 1442 North Third, Abilene, Texas.
Dr. John Cunningham Montgomery, Jr., 202 Fine Arts Bldg., Bellingham, Wash.
Dr. Arthur James Moss, 239 North Locust St., Inglewood, Calif.
Dr. Aaron Nisenson, 6230 Wilshire Blvd., Los Angeles, Calif.
Dr. Leon Oettinger, Jr., 4614 Sunset Blvd., Los Angeles, Calif.
Dr. Sam M. Powell, Jr., 1611—5th St., Corpus Christi, Texas.
Dr. A. Martin Puris, 4753 N. Broadway, Chicago, Ill.
Dr. Edgar Moskedal Rector, 4212 N.E. Broadway, Portland 13, Ore.
Dr. Francis H. Redewill, Jr., 124 E. Hadley Street, Whittier, Calif.
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Dr. Catherine Foss Roberts, 1629 Selby Avenue, Los Angeles 24, Calif.
Dr. Samuel M. Rosenthal, 6333 Wilshire Blvd., Los Angeles 36, Calif.
Dr. Melvin H. Schwartz, 1904 Franklin Street, Oakland, Calif.
Dr. Albert John Sheldon, 1524 N. Broadway, Santa Ana, Calif.
Dr. Ralph Omer Sherberg, 508 Metropolitan Bldg., Denver 2, Colo.
Dr. Frederic E. Simpson, 234 W. Beauregard, San Angelo, Texas.
Dr. Pauline George Stitt, Territorial Dept. of Health, Honolulu, Hawaii.
Dr. Philip Roger Vandeman, General Delivery, Olympia, Wash.
Dr. James Sherman Vedder, Marshfield Clinic, Marshfield, Wis.
Dr. Elsie I. Wisczorowski, 645 Fullerton Pkwy., Chicago 14, Ill.

A postgraduate course in pediatrics was given by the Pediatric Department of the University of Arkansas School of Medicine under the direction of Dr. Wm. A. Reilly, Professor of Pediatrics, Nov. 4 to 6, 1948. Guest speakers were Dr. Waldo E. Nelson, Professor of Pediatrics, Temple University, Philadelphia, Pa., and Dr. Arild E. Hansen, Professor of Pediatrics, University of Texas, Galveston, Texas.

Book Reviews

Ensayo Estadístico sobre Valores Sanguíneos en Lactantes Sanos y Enfermos.* J. J. Murtagh, C. E. Martinez Castro Videla, R. M. Ferro, and H. C. Ferro. Buenos Aires, Argentina, 1947, Libreria y Editorial "El Ateneo," pp. 150, 77 tables, and 10 charts; 205 references.

This monograph reports the results of a survey of several hematologic and blood chemical constants in infants under one year of age. The aim was to determine whether or not normal values derived from European and North American populations are applicable to infants in the Argentine.

The hematologic survey is limited to the concentration of hemoglobin, dimensions of the red cells, and the red cell-hemaglobin relations as currently measured or calculated. The blood chemical constituents considered are serum protein; whole blood nonprotein nitrogen and its separate components; whole blood, serum, and erythrocyte chlorides; and the carbon-dioxide combining power of the serum.

The report is divided into three parts: first, a review of the literature relating to the foregoing items; second, the authors' observations on healthy breast-fed and bottle-fed babies; third, their observations on dehydration and other disturbances of the acid-base equilibrium.

The monograph is, in most respects, a model to be imitated. The review of the literature is comprehensive and clear; original data are presented in a compact, understandable manner. The authors are to be congratulated especially on their recognition of the need to analyze the data statistically by the small-numbers method, and on the clarity of their presentation of the theoretical and practical aspects of this technique.

No claim for originality is made; hence, the reader will not be surprised to find only that many firmly established conclusions have been reaffirmed. Nonetheless, original, reliable data are always of value in evaluating the details of homeostasis throughout the world. It is only to be regretted that the investigators did not find it possible to make their blood chemical studies more complete.

D. McC.

Diseases of the Ear, Nose and Throat. William Wallace Morrison, M.D., Professor of Otolaryngology and Attending Otolaryngologist, New York Polyclinic Medical School and Hospital. New York, 1948, Appleton-Century-Crofts, Inc., 772 pages, 359 illustrations. Price $8.50.

This is a completely new successor to Morrison's previous book under a different title. It is intended as a student textbook and covers the entire field of otolaryngology. The material is well presented, making for easy reading. The illustrations are schematic which aids in the reading matter. Method of examination is explained. Each subject was delved into rather sufficiently and the material has been brought up-to-date. Newer modes of therapy have been included. Operative techniques are discussed enough to enlighten practitioners as to what is done to their patients. It should be a valuable aid to the student and practitioner of medicine as well as an added book on the shelf of practicing otolaryngologists.

CUTLER.

*A Statistical Study of Blood Constituents in Healthy and Sick Infants.

Editor's Column

DEATHS IN CHILDREN DUE TO ACCIDENT

The developments of medical science in the last quarter century have made many striking changes in mortality statistics. Deaths from diarrheal diseases, for example, decreased 91 per cent between 1930 and 1946 in the 1- to 4-year age group, and deaths due to communicable diseases in the 5- to 9-year age group came down 83 per cent. The total reduction in deaths from disease has resulted in accidents becoming the leading cause of death in children. At present about 5,000 children in the 1- to 4-year age group die annually from accidents. Burns cause the largest number of fatal accidents occurring in the home, and motor vehicle accidents are the chief cause outside the home.

It has become almost impossible to pick up a daily newspaper in our metropolitan areas without reading of the death or serious injury of some child due to an accident in the home or on the street. In an effort to reduce accidental deaths in children an educational campaign in accident prevention which should receive the support of every physician is now under way.

While most accidents in young children are due to carelessness and hence are preventable, a most interesting development in connection with the study of the cause of accidents has been the recognition in recent years of what is known as accident-proneness. It has been conclusively shown that certain individuals are especially prone to accidents. Our present knowledge of the subject was reviewed in an interesting article by Bakwin and Bakwin in the June issue of the JOURNAL (**32**: 749, 1948). While the studies so far have been chiefly in the adult field, accident-proneness undoubtedly exists in children. In Rochester, N. Y., a special clinic has been opened to study accident-prone children. It is a new field of medical study with whose developments the physician must keep abreast.

A QUESTION OF SEMANTICS

Attracted by the subject, "Should Sex Education Be Taught in the Public Schools," we tuned in a few weeks ago to a national radio program of supposedly high educational value. It was one of the most stupid debates imaginable. The debaters had quite different things in mind by the term "sex education," and hence the pro and con arguments were quite beyond point and could only leave an uninformed listener in a bewildered state of mind. It was a striking example of the futility of an argument when the question is indefinite and undefined. It reminded us of most of the many discussions over "socialized medicine" in recent years. Whenever we are asked what we feel about "socialized medicine," we ask the questioner to please define exactly what he means by the term. The usual result is that there is very little left for argument, and the conversation turns to one of an amicable discussion of the complex medical problems facing the public and the physician.